Neurology

OFFICIAL JOURNAL OF
THE AMERICAN ACADEMY OF NEUROLOGY

JULY · AUGUST · 1951
Volume 1 · Number 4

"Good to excellent results with PROTAMIDE"

. . . In 28 Cases of HERPES ZOSTER at Bethesda Naval Hospital*

William C. Marsh, Commander (MC) U.S.N., in a currently published paper[1], "Treatment of Herpes Zoster with Protamide," now available to physicians as a reprint, presents these findings:

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"The advantages of Protamide are the simplicity and absence of pain in administration, lack of reactions, and apparent safety.

"Costello[2] found that Protamide was effective in the relief of the posterior root pain of tabes dorsalis."

* *U. S. Naval Hospital, National Naval Medical Center, Bethesda, Maryland.*

1. U.S. Armed Forces Med. Journal, September, 1950.

2. Costello, R. T. New treatment for "lightning pains" of tabes dorsalis, Urol. and Cutan. Rev. 51: 260-263, May, 1947.

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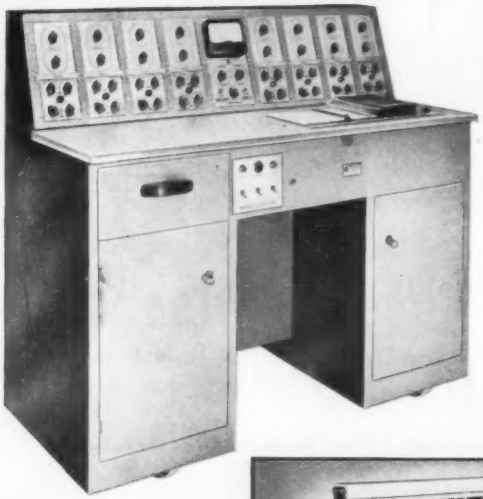

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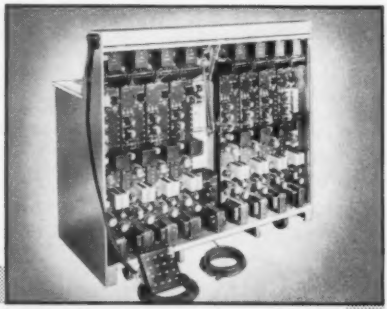

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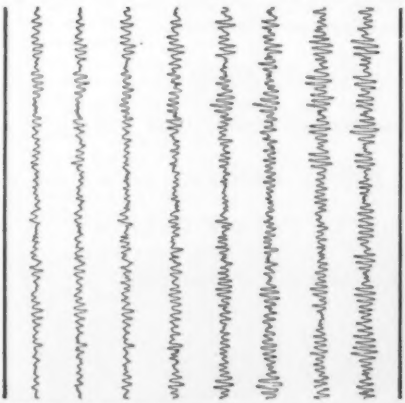

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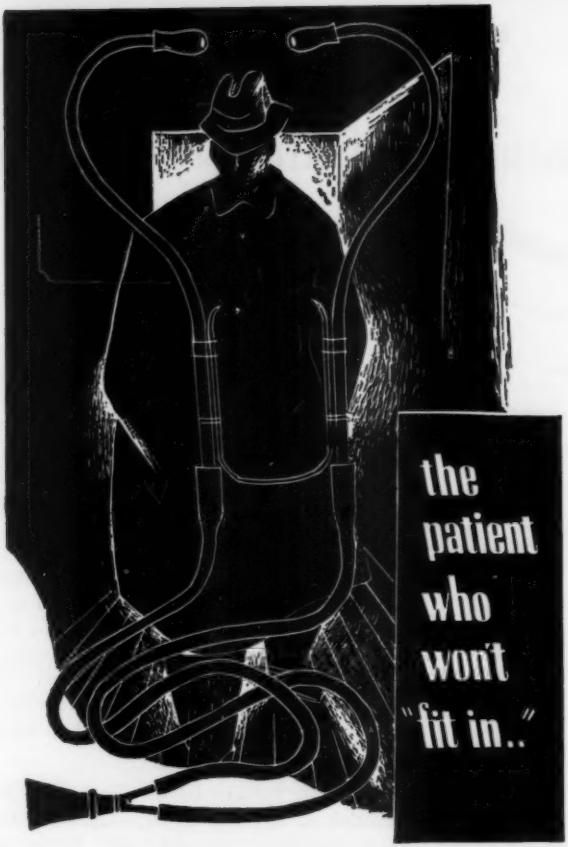

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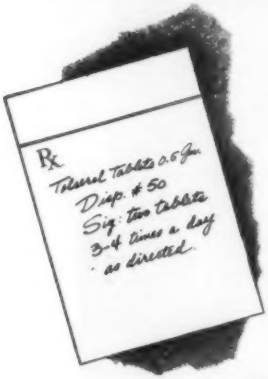

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Contents · JULY-AUGUST, 1951

Clinical Aspects of Cerebral Anoxia in Man
A. THEODORE STEEGMANN, M.D. 261

Surgical Treatment of Postherpetic Neuralgia by Subdermal Denervation
KENNETH H. ABBOTT, M.D. AND BRUCE C. MARTIN, M.D. 275

Alterations of Cerebral Functions in Pheochromocytoma
NATHANIEL S. APTER, M.D., WARD C. HALSTEAD, PH.D., ALF S. ALVING, M.D., PETER J. TALSO, M.D. AND THEODORE J. CASE, M.D. 283

Electroencephalographic Findings in Post-Traumatic Encephalopathy
ANDRE A. WEIL, M.D. 293

Intravenous Sodium Amytal in Generalized Language Dysfunction
GEORGE N. RAINES, M.D. AND ROBERT COHN, M.D. 299

Electroencephalographic Foci in Temporal Lobes With Consideration of Seizure Manifestations
CHARLES W. IOBST, M.D. AND FRANCIS M. FORSTER, M.D. 309

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Contents—*Continued*

Sequelae of Western Equine Encephalitis
DONALD W. MULDER, M.D., MURIEL PARROTT, M.A. AND MARGARET THALER, M.A. 318

Treatment Review

Treatment of Headache
ARNOLD P. FRIEDMAN, M.D. 328

Clinical Pathologic Conference

Presented by CHARLES RUPP, M.D. AND HELENA E. RIGGS, M.D. 335

Book Reviews 338

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Neurology

Clinical Aspects of Cerebral Anoxia in Man

A. Theodore Steegmann, M.D.

THE availability of oxygen under normal circumstances has made it unnecessary for living organisms to develop physiologic processes that will sustain cellular respiration under conditions of oxygen lack. When deprivation of oxygen occurs during various abnormal conditions the margin of safety is narrow and an emergency situation arises in a matter of minutes.

Studies of cerebral blood flow in man by various techniques[1-3] are not in complete agreement, but in general indicate that approximately 700 to 1,000 cubic centimeters of blood flows through the brain each minute. Since the cardiac output at rest is about 4 liters per minute, it appears that the brain, representing only about 2 per cent of the body weight, receives 20 to 25 per cent of the output of the left ventricle.

Brain tissue needs an excessive blood supply because it has a high metabolism, requires an abundance of oxygen and is the most sensitive of all tissue to oxygen lack.[4] Carbohydrate or a derivative is the principle source of energy in the brain. Since there is very little glycogen present and probably very little glycogenesis or glycogenolysis, glucose derived from the blood is the principle carbohydrate used.[5, 6]

There is both clinical and experimental evidence[7-9] that the cerebral cortex cannot withstand complete oxygen deprivation for much more

From the department of neurology, University of Kansas School of Medicine, Kansas City, Kansas.

than five minutes without undergoing irreversible degenerative changes. The corpus striatum in man is almost equally vulnerable, but the midbrain and medulla are more resistant. The fact that the respiratory and circulatory regulating centers in the medulla can resist anoxia longer permits survival for a variable period of time after the cortex is damaged irreparably. Residual symptoms that develop after restoration of the medullary centers depend on the extent and degree of damage to the more vulnerable areas. When these symptoms are produced by reversible nerve cell damage, recovery is possible and may occur without clinical evidence of residual injury. In fact, symptoms apparently can indicate injury out of proportion to that actually present. Variation in the type of symptoms reflects the degree and distribution of cerebral dysfunction, but the actual degree of pathologic damage depends on severity of anoxia, its duration and the method by which it is produced. The differences in tissue reaction to anoxia produced by gradual or temporary cutting off of the oxygen supply by arterial constriction has been studied by Becker.[10] There are also differences in the ability of certain individuals to withstand anoxia, but the exact reason for this is not understood.

Before considering the various types of anoxia and the symptoms produced, the terms used in description of anoxic states need clarification. Dorland[11] defines "anoxia" as "oxygen deficiency, oxygen lack, a condition in which the cells of the body do not have or cannot utilize sufficient oxygen (O_2) to perform normal function." Fortunately this comprehensive definition is coming into more universal use. "Hypoxia" is defined as "low oxygen content or tension; deficiency of oxygen in the inspired air." It can be seen that a part of this definition assumes that the oxygen deficiency is in the inspired air, an assumption not implied by the term "anoxia." "Asphyxia" means "suffocation; also suspended animation from suffocation. It is a condition in which there is anoxia and increased carbon dioxide tension in the blood and tissues. It is attended by a feeling of suffocation and coma." This definition specifies that hypercapnia or increased carbon dioxide is present in asphyxia. It should be kept in mind that in some anoxic states hypercapnia is not present. The term "anoxemia" or "hypoxemia" are seldom misused since they indicate correctly that the oxygen deficiency is in the blood. "Ischemia" means "local or temporary deficiency of blood chiefly due to contraction of a blood vessel," but the term "local anemia" is used in the same sense and "may be due to mechanical interference with the blood supply by compression of a vessel, embolism, spasm, etc."

Barcroft[12] recognized three types of disturbance in the physiology of respiration that lead to anoxia. The first or *anoxic type* is characterized

by low oxygen tension in the inspired air leading to inadequate oxygenation of the blood. Since this type of anoxia has to do with aeration of the blood in the alveoli it would seem that the term "alveolar anoxia" would be appropriate, but such a term has not been used. The second or *anemic type* is the result of a deficient amount of hemoglobin in the blood or an inadequate quantity of blood necessary to carry sufficient oxygen, though the amount of oxygen in the inspired air is adequate. Anemic anoxia may occur in the presence of an adequate amount of hemoglobin if the hemoglobin is bound by another gas such as carbon monoxide which prevents the hemoglobin from taking up its full quota of oxygen. In this paper an ischemic process will be considered equivalent to anemic anoxia. A third or *stagnant type* is produced by a general retardation or inadequacy of the general circulation. The blood is aerated in the lungs but tarries in the capillaries and surrenders a large part of its oxygen. Therefore, the minute volume of oxygen laden blood supplied to the tissues is low. This occurs in anesthesia, cardiac failure and low blood pressure during shock. Peters and Van Slyke[13] described a fourth type, the histotoxic type in which cellular respiration is reduced or abolished because of the action of toxic substances in the cell which inhibit intracellular biochemical oxidative processes. Cyanide poisoning is an example.

Anoxic states in man arise in various ways, and a combination of the above-described types of anoxia may co-exist. In drowning and electric shock anoxic anoxia is produced by respiratory paralysis and apnea. Respiratory failure occurs in morphine poisoning, but there is also a cytotoxic anoxic factor and the low blood pressure present reduces cerebral circulation thereby contributing to a stagnant anoxic state. In choking and strangulation there is rapid depletion of alveolar oxygen. Hanging or cervical constriction combines anoxic anoxia with anemic anoxia, the latter because of compression of the cervical arteries. Aeration in the pulmonary alveoli may be hindered by the inhalation of smoke or irritant gases. Pneumonia or pulmonary edema may have the same effect. Pulmonary embolism leads to ischemia of the pulmonary circulation with resulting anemic anoxia. In severe concussion of the brain, anoxia may contribute to the serious outcome. There may be cardiac failure and peripheral vasodilatation following injury to the vasomotor center and anoxia secondary to failure of the respiratory center.[4] In the cerebral vessels, vasodilatation stasis and edema combine to produce anoxemia.[14] Here we see the anoxic, anemic and stagnant types all playing a role. Paralysis of the bulbar centers and thoracic musculature in poliomyelitis can produce anoxic encephalopathy.[15] The best example of cytotoxic anoxia is cyanide poisoning, but a cytotoxic factor plays a role in intoxi-

cation by alcohol, morphine and sedatives (barbiturates, chloral), which in addition produce anoxia by depression of the medullary respiratory and circulatory centers.

Damage to the brain following anesthesia with nitrogen monoxide and other general anesthetics has been studied extensively in recent years.[7, 16-20] In many cases the patient had a respiratory arrest. Some patients had a cardiac arrest simultaneously, or the cardiac arrest followed respiratory failure. If overventilation precedes this serious event, the resulting low carbon dioxide level of the blood deprives the respiratory center and the cerebral circulation of its best stimulant, namely, carbon dioxide. If anoxia endures long enough or is of severe enough degree, the result is a permanent injury to the cortex and corpus striatum. Restoration of cerebral function after prolonged cardiac arrest has been reported by Fox.[21] In his case, cardiac arrest lasted for 27 minutes. Circulation was maintained by cardiac massage and artificial respiration. Spontaneous heart action was restored after intravenous Procaine injection. The patient had prolonged coma, confusion and irritability for two days. This was followed by impaired visual acuity and asphasic disturbances which recovered completely after five months.

Spinal anesthesia also has been responsible for cerebral damage. The respiratory physiologic functions are disturbed by such factors as the drop in systemic blood pressure following vasodilatation by sympathetic block, sympathetic block of the heart and adrenals, loss of skeletal muscle tone, diminished respiratory activity by intercostal paralysis, low blood volume before operation, and actual depression of the medullary respiratory center.[22-24]

Anoxia occurring in high altitude flying assumed great importance during World War II and has stimulated interesting physiologic and clinical studies.[25-27] Besides anoxic anoxia, nitrogen gas embolism complicates the condition in altitudes above 30,000 feet (9,144 meters). Gas embolism is thought to induce local ischemia and vascular spasm.

In carbon monoxide poisoning anemic anoxia is produced by the formation of carboxyhemoglobin which binds the hemoglobin and interferes with its function of combining with oxygen. Victims of carbon monoxide poisoning overventilate and develop acapnia which contributes to the early depression of the respiratory and circulatory centers.

In artificial fever therapy relative anoxia may be produced by elevated temperature which reduces the oxygen saturation of the blood and increases the velocity of capillary circulation. This leads to alkalosis, which decreases the readiness of hemoglobin to surrender oxygen to the tissues.[14]

The etiology of anoxia in the newborn is complex and originates out of one or more of the physiologic types of anoxia. Snyder has reviewed the subject excellently.[28] He points out that asphyxia in the newborn is caused principally by prematurity of the fetus, trauma and analgesia. Among the traumatic factors occurring before, during or after birth, he mentions impaired circulation of the cord by compression or placental separation, uterine tetany, narcosis, prolonged pressure on the head, cerebral vascular injury, premature respiratory effort and forcible methods of resuscitation. Anesthetics and analgesics such as morphine depress fetal respiration and prolong labor in the mother, which in turn leads to fetal anoxia. Atelectasis may be produced by asphyxia or by obstruction of the air passages. Apnea in the newborn is of three types, namely, anoxemic, acapnic and anesthetic. The fetal respiration depends on both oxygen and carbon dioxide in the fetal blood. Oxygen want depresses respiratory movements and a lack of carbon dioxide also leads to apnea. Unlike the reaction in adults, an excess of carbon dioxide produces no effect on the fetus. Snyder found that in rabbit fetuses the chemoreceptors of the carotid body do not function before birth. The fetal respiratory system is more sensitive to narcosis than that of the adult, but is more resistant to anoxia. Giaja and Markovic[29] attribute this to the facility with which newborns develop a lowering of body temperature during hypoxia, which protects them against anoxia. The fetus differs from the adult in another respect in that anoxia produces bradycardia rather than tachycardia.

Investigations of the physiology of anoxia indicate that in certain individuals hemoconcentration occurs with contraction of the spleen and a resulting increase of red blood cells and hemoglobin in the blood. The heart rate, blood pressure and cardiac output are increased at first, but with more severe degrees of anoxia the cardiac output is reduced, the blood pressure falls, venous pressure rises and cardiac arrythmias appear. When oxygen in the inspired air is reduced below 9 per cent, cardiac arrythmias are followed by heart failure and death. The heart seems to be more susceptible to anoxia than the rest of the circulatory apparatus. An early rise in blood pressure due to anoxia is explained by stimulation of the carotid and aortic chemoreceptors which activate the vasomotor centers by way of their neural connections with the medulla. Carbon dioxide does likewise by a direct effect. The respiration is increased in volume and rate. The blood glucose level rises, apparently as the result of adrenal stimulation. This can be prevented experimentally by adrenalectomy. In histotoxic anoxia both respiratory and cardiac failure occurs rapidly. The kidney can withstand considerable anoxia, but in severe

anoxia urinary secretion is diminished, acidosis develops and the body temperature falls. In the central nervous system anoxia causes vasodilatation and an increased blood flow in the medulla and hypothalamus. It also stimulates the vomiting mechanisms. The respiratory and vasomotor medullary centers are stimulated by an increase of carbon dioxide and by a reduction of oxygen, the latter effect by reflex stimulation of the chemoreceptors. When the chemoreceptors are removed oxygen lack has a depressing effect.[30] There is also the possibility that the hypothalamus may be stimulated in anoxic states.

It can be concluded after a consideration of all of these factors that anoxia in man is rarely a simple process, either in its mode of production or its physiologic effects. Therefore it can seldom be classified according to pure physiologic types.

The symptoms of anoxia appear rapidly without warning but depend upon the degree and duration of oxygen lack. Since the cortical centers are particularly vulnerable, the nerve cells show rapid dysfunction. Some of the symptoms represent a decrease in neuronal function and others belong to the release category. The symptoms can be divided into those of (1) sudden complete anoxia, (2) partial anoxia and (3) anoxic encephalopathy.

COMPLETE CEREBRAL ANOXIA

Perhaps the most sudden and complete anoxic states studied in man were the ingenious experiments of Rossen, Kabat and Anderson.[1] These investigators produced an almost instantaneous complete cerebral anemia by a specially designed pressure cuff applied to the lower cervical region. This abolished the blood supply to the carotid and vertebral arteries without restricting respiration. This procedure does more than deprive the tissues of oxygen, since it also cuts off the supply of nutritive substances in the blood and prevents the carrying away of tissue metabolites. Normal young subjects were observed for periods up to 10 seconds and schizophrenic patients for periods up to 100 seconds. Fixation of the eyes occurred within five to six seconds. This was followed by blurring of vision, constriction of the visual fields, and in some subjects paresthesias or shooting pains in the extremities. Loss of consciousness took place in six to 10 seconds. It should be pointed out here that in the anoxic anoxia of high altitude flying, unconsciousness does not happen until after three minutes at 35,000 feet (10,668 meters) or until after one minute at 40,000 feet (12,192 meters). Loss of consciousness was followed by a generalized tonic clonic convulsion that lasted six to eight seconds. This occurred after the pressure cuff was released upon the beginning of unconscious-

ness. After the return of consciousness the subject showed a variable reaction for 15 to 20 seconds. This was described as confused, dazed, excited, euphoric or fearful. There was only a slight sinus slowing or no change in the electrocardiographic tracings. The electroencephalogram exhibited sudden large slow waves that corresponded to the period of eye fixation or loss of consciousness. In patients subjected to cerebral anemia for periods as long as 100 seconds, the loss of consciousness was accompanied by cyanosis and convulsions. In some patients involuntary urination or defecation occurred in 15 to 40 seconds. Bradycardia appeared after 20 to 30 seconds, there was a 15 per cent rise or fall of systolic blood pressure, the pupils dilated and the corneal reflexes disappeared, the latter within 10 seconds. Abdominal reflexes disappeared only after prolonged anoxia and reappeared more slowly than the corneals. The signs of Babinski, Rossolimo and Hoffmann could be elicited in some cases. Respiration was increased in rate and amplitude. After restoration of the cerebral blood flow, flushing of the face preceded the return of consciousness. Individual resistance to anoxia varied, but all individuals tested in the experiments recovered promptly and suffered no residual symptoms.

PARTIAL CEREBRAL ANOXIA

The symptoms of partial anoxia vary greatly but have some similarities to those of complete cerebral anoxia. The onset of unconsciousness is delayed and consequently more time is allowed for the development of symptoms. In simulated high altitude, the anoxic anoxia produced before the critical level of 30,000 feet (9,144 meters) is little complicated by other factors. Above 30,000 feet there is an increase in volume of the gas-containing organs, and decrease in the solubility of gaseous nitrogen in the body fluids which leads to the development of air bubbles in the blood and tissues. Air embolism which induces vasospasm leads to focal neurologic symptoms and signs. The cerebral anemia that follows acceleration or deceleration during rapid changes of direction in flight at high speed induces blackouts, convulsive movements and retrograde amnesia. Anemic anoxia must contribute to these symptoms. Long exposure to partial anoxia has led to fatigue syndromes in flying personnel. These cannot be explained entirely on the basis of anoxia, however.

The symptoms of partial cerebral anoxia may be divided into the following categories: (1) psychic changes, (2) sensory defects, (3) motor symptoms, (4) defects in coordination and (5) physiologic changes.

Psychic changes. In altitudes between 10,000 feet (3,048 meters) and 14,000 feet (4,267 meters) the psychic changes vary in individual cases. Some show a happy euphoric mental state while some experience depression accompanied by fear and anxiety. Others exhibit lassitude, somnolence and a slight headache. When an altitude over 14,000 feet is reached the intellect becomes less keen, judgment is disturbed and a person may cling to ideas stubbornly. Emotional instability or outbursts, amnesia, disorientation, confusion and aphasia have been observed. Headaches of a migraine-like character have been reported, but this may not be the result of anoxia alone. Unconsciousness occurs at 35,000 feet (10,668 meters).

Sensory defects. Of the special senses, the most striking changes occur in the visual system. These include blurring, scotoma, interference with depth perception and loss of vision. These symptoms have been observed above 14,000 feet (4,267 meters). Changes in general sensation consist of paresthesias, itching and neuralgia. Above 14,000 feet the response to painful stimuli may become diminished.

Motor symptoms. The early stages of anoxia are characterized by restlessness or muscle twitching. Above 14,000 feet paresis of the limbs, neck and trunk muscles takes place, and at higher altitudes the muscle tone is reduced and dyskenesias develop. Convulsions occur at altitudes above 30,000 feet (9,144 meters).

Defects in coordination. When an altitude of 14,000 feet or above is reached ataxia, incoordination and difficulty in writing have been observed.

Physiologic changes. The skin may be pale, cold and moist. Cyanosis may or may not be present. Oximetric studies show that anoxia can occur without cyanosis. In carbon monoxide poisoning the skin and mucous membranes develop a cherry-red tinge. The pupils and the retinal arteries dilate. Respiration increases in depth between the altitudes of 7,000 feet (2,134 meters) and 10,000 feet (3,048 meters), and the rate is increased after 15,000 feet (4,572 meters). If the increased rate produces hypercapnia, reduced carbon dioxide tension diminishes stimulation of the respiratory center and leads to Cheyne-Stokes respiration. Above 25,000 feet (7,620 meters) a respiratory and circulatory crisis develops in some individuals resulting in respiratory and cardiac failure. Heart failure may follow vagal slowing with decreased systolic pressure, increased venous pressure and impaired coronary blood flow. Nausea and vomiting are common in altitude sickness. The red blood cell count and hemoglobin increase but the alkaline reserve of the blood may be diminished pro-

vided there is a decrease of carbon dioxide which leaves the blood more alkaline. The alkaline base is then excreted by the kidneys.

At altitudes over 30,000 feet (9,144 meters) air embolism complicates the picture. The person may then show hemianopsia, loss of sensation or paralysis of one or more limb, shock, collapse, unconsciousness and convulsions. Gas bubbles may induce severe pain in the eyes, ears, joints or abdomen.

ANOXIC ENCEPHALOPATHY

The diversity of causation can be illustrated by some key references. These include delayed death after hanging,[31, 32] following carotid artery ligation,[31, 33] after strangulation,[34, 35] following Trendelenburg's operation for massive pulmonary embolism,[36, 37] after anesthesia,[7, 16-24] in carbon monoxide intoxication, [38-42] in high altitude flying[43-46] and after respiratory difficulty in poliomyelitis.[15] It is beyond the scope of this paper to review the differences in the clinical manifestation of the patients described in these reports. On the other hand, the striking similarity of the symptoms regardless of the method by which anoxia is produced should be emphasized.

The symptoms may be divided into five groups: (1) disturbance in consciousness; (2) psychic changes; (3) visual and sensory defects; (4) motor symptoms which are cortical, extrapyramidal and decerebrate in nature; and (5) changes in respiratory and autonomic functions.

Disturbance in consciousness. In practically all types of severe oxygen deprivation associated with brain damage, unconsciousness is profound and frequently prolonged for a number of hours. In fatal cases consciousness may never be regained. Stupor is interrupted at intervals by delirium or noisy maniacal behavior. No sharp line of demarcation can be drawn between the disappearance of this state and less severe symptoms that emerge in patients who survive longer. Symptoms may be transitory, persistent or recurrent depending upon the degree of cerebral damage and the distribution of the pathologic process.

Psychic changes. On emerging from coma or delirium some patients are unable to speak or comprehend. The sensorium is cloudy or disoriented and the speech slurred, incomprehensible or aphasic. Other patients exhibit silly and childlike behavior. Later memory defects and variable degrees of dementia remain permanently. Peculiar emotional changes materialize and so closely resemble hysteria that an erroneous diagnosis is frequently made. Emotional lability, screaming, laughing, crying or intervals of apprehension and fear characterize this state. Con-

tinuous talking or singing may go on for hours at a time or the patient may show negativism or stubbornness.

Visual and sensory defects. Alteration in visual function is a remarkably constant symptom in severe anoxic states. In severe cases the eyes are wide open and roam about. Blindness may be complete even for light perception and is presumed to be the result of both central and peripheral damage. There may be scotomata, constriction of the visual fields, homonymous field defects or changes in color perception in individual cases. The pupils have most often been described as dilated or dilated and fixed. The optic discs are usually normal, but pallor has been recorded.

Disturbances in general sensation are notably uncommon. Often they represent subjective complaints rather than demonstrable changes. Reports in the literature mention left sided numbness, pain in the hands, numbness and tingling of various parts of the body, paresthesias, loss of vibratory sense perception and Romberg's sign. An accurate sensory examination may be impossible in some cases because of the psychic changes or disturbed state of consciousness.

Motor symptoms. Convulsions, usually recurrent, are the most striking motor manifestations during the period shortly following the anoxic injury. These may come and go for hours. They are accompanied by extensor tonus of limbs and trunk and are both tonic and clonic in character. Muscular twitching or generalized tremor may be an associated, rarely an isolated, symptom. Convulsions are frequently followed by waves of restlessness accompanied by emotional changes or delirium. Nystagmus or conjugate ocular deviation is present in some cases. Upon recovery from these severe symptoms the patient may be speechless or unable to swallow. One or more of the limbs may be spastic and paralyzed. Apraxia in carrying out movements has been observed, and the gait may be spastic or ataxic. Brain damage tends to be bilateral but focal signs may be more pronounced on one side. Hemiplegia with lower facial weakness and slow dysarthric, incomprehensible speech has been described. Isolated cranial nerve palsies are extremely rare since the brain stem and medulla are resistant to anoxia. Changes in tendon reflexes correspond to physiologic motor dysfunction. They may be in shock early, later exaggerated and accompanied by clonus. The abdominal reflexes are correspondingly absent. Pathologic finger and plantar responses are present when the pyramidal system is sufficiently damaged.

Since the corpus striatum like the cortex is vulnerable to anoxic damage, symptoms of the extrapyramidal motor type are encountered frequently. Restlessness and thrashing about often accompany the stuporous

periods, but movements may take on a more distinctly choreiform or choreo-athetoid character. There may be facial grimacings, pursing of the lips, chewing movements or grinding of the teeth. That some of these patterns are cortical (premotor) seems self-evident. Extrapyramidal motor symptoms in patients with long survival may persist as choreiform, athetoid or parkinsonian syndromes.

Decerebrate rigidity showing marked extensor tonus (opisthotonos), and sometimes Magnus and DeKleyn type of brain stem reflexes, have been described following severe cerebral damage and decerebration of higher levels. However, decerebrate states may be physiologic and recoverable as in the case of Lenahan and Reed.[47]

Cerebellar signs including nystagmus, action tremor, incoordination, ataxic gait and hypotonia have been reported.

Changes in respiration and autonomic functions. During the early and acute phases of oxygen deprivation, respiratory failure or cardiac arrest may first call attention to the serious complication especially during anesthesia. Respiratory failure is the most common event, but both respirations and pulse may stop simultaneously or cardiac arrest may follow respiratory failure. It cannot be said with certainty that anoxia is the sole cause of cardio-respiratory failure in anesthesia, but it can be said positively that once it has occurred severe anoxia develops quickly and the interval of survival is entirely dependent upon immediate restoration of oxygen supply to the brain. Death has occurred many times at this stage, especially when cardiac function could not be restored. After the circulation and respiration are revived, respiration may be irregular and vary in rate and amplitude. Periods of apnea or Cheyne-Stokes breathing necessitate constant vigilance of the patient. The blood pressure and pulse rate also fluctuate widely, and there is vomiting and involuntary action of bladder and bowel. The temperature is moderately elevated, but in fatal cases may rise terminally to 108° F. (42.20° C.) or higher. The skin is pale, cyanotic or in carbon monoxide poisoning a cherry-red hue. In some cases the face is abnormally flushed. Sweating may be profound.

The only laboratory observations of importance are leukocytosis which varies from 12,000 to 20,000 white cells per cubic millimeter of blood and an elevation of the pressure of the cerebrospinal fluid. This is rarely over 300 millimeters of water pressure.

It must rest on future research and further knowledge of cerebral function to explain some observations in anoxic encephalopathy that are as yet obscure. The explanation of fluctuation of symptoms in cases with apparently healed residual damage is inadequate. Whether this rests on vasomotor factors as Courville has suggested or is dependent on

differences of threshold responses of the damaged cortical neurons still belongs to the realm of speculation. Also it is not clear why so many autopsied cases demonstrate erosion of the gastrointestinal tract. Of four cases of postanesthetic encephalopathy studied personally, one patient passed blood from the bowel, but an autopsy was not permitted except on the brain; two others had hemorrhagic erosions of the gastric mucosa.[7] It seems possible that these changes may be dependent upon and secondary to degeneration of the central nervous system, although damage to other tissues by anoxia has to be considered. Ulceration of the gastrointestinal tract occurs in shock,[4] but anoxia seems to play a role in shock. Gastric erosions have also been described as a part of the "adaptation syndrome"[48] and following disturbance in interbrain autonomic regulation.[49]

There is still a great need for detailed clinical studies on cases of postanoxic encephalopathy in the residual stage. Until a sufficient number of such cases have been recorded in the literature, an adequate detailed clinical classification will not be possible. On the basis of the symptomatology described above the following clinical classification is suggested.

I. Primarily Cortical Defects
  1. Diffuse
    a. Emotional instability
    b. Psychotic behavior
    c. Dementia
  2. Focal
    a. Visual defects (central blindness, scotomata, etc.)
    b. Cerebral diplegia
      symmetrical or asymmetrical,
      with or without minor sensory changes
    c. Speech defects (dysarthria, aphasia)
    d. Frontal ataxia or tremor

II. Primarily Extrapyramidal Motor Defects
  1. Paleostriatal
    a. Parkinson-like syndromes
    b. Bradykenesia without tremor
  2. Neostriatal
    a. Athetosis
    b. Choreo-athetosis

III. Mixed Forms
  Variable combinations of I and II

SUMMARY

1. The principal causes of anoxia in man and the physiologic effects of oxygen deprivation are reviewed.

2. The symptoms resulting from complete cerebral anemia, partial cerebral anoxia and anoxic encephalopathy are described.

3. A clinical classification of anoxic encephalopathy in the residual stage is presented.

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Surgical Treatment of Postherpetic Neuralgia by Subdermal Denervation

Kenneth H. Abbott, M.D. and Bruce C. Martin, M.D.

RELIEF of intractable and at times intolerable postherpetic neuralgia, commonly seen in the aged and lasting frequently until the patient's demise, has long been sought. The multitude of therapeutic agents,[1] including surgical procedures, that have been attempted to give these sufferers relief indicates the lack of any dependable medical or surgical therapy in this distressing syndrome. This preliminary report presents the results of surgical treatment of three patients with postherpetic neuralgia involving the spinal nerves. Patients were treated by elevation of skin flaps, based caudally, down to the fascia over muscle over the entire herpetic scarred area. Each of these patients had had numerous types of medical and injection treatments and had failed to respond to any therapy. Satisfactory results obtained by the methods outlined here indicate that a preliminary report is justified.

Attacking the problem of postherpetic pain by focusing attention upon the skin is not a new idea; in fact, since antiquity various medications have been applied to the skin in an attempt to give relief. Even the surgical approach directed to the skin in the hope of relieving the postherpetic neuralgia is not new, for Gowers[2] stated, "Sir William Jenner in his lectures was accustomed to illustrate the obstinate persistence of this pain in the old by the instance of a man who, before the days of anesthetics, endured the excision of the skin to which the pain was referred in the hope of relief but found none, and then, unable to bear the continuous agony, shot himself."

In more recent years efforts toward temporary chemical denervation of the skin have been reported by Hallander[3] and by Secunda, Wolf and Price,[4] who used Novocain and various substances such as anesthetic

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agents in oil (Nupercaine, Hallander's formula, and a modification of Hallander's formula containing benzocaine, benzylalcohol, phenol and oil of sweet almond). In acute herpes zoster these medications and also x-ray therapy[5] have proved successful, but for the most part they have failed to relieve postherpetic neuralgia. Likewise paravertebral block[6, 7] with anesthetic agents has given good results in acute herpes zoster but has resulted in only temporary relief in postherpetic neuralgia. Undoubtedly sympathetic block alone has been carried out by many surgeons, but there are few references to this procedure in the literature.[8, 9, 10, 11] More recently, generalized sympathetic block by intravenous medication has been used employing tetraethylammonium chloride and related chemical compounds.[12, 13] Although the causalgic pain in acute herpes zoster has responded very well to this therapy, relief from pain has been transitory in postherpetic neuralgia.

The surgical treatment of postherpetic neuralgia, aside from that of Jenner,[14] has consisted of posterior root rhizotomies and cordotomy which have been notoriously unsuccessful.[15, 16, 17, 18, 19] Nevertheless, Hyndman[16] reported successful relief from postherpetic neuralgia following rhizotomy, although he points out that rhizotomy must be carried out over a wider area than that which is commonly used if relief is to be obtained by this means, that is, rhizotomy of two or three segments above and similarly of two or three segments below the involved segments. Kahn[18] and others have demonstrated that anterolateral cordotomy has been a complete failure in the relief of postherpetic neuralgia. Peet[19] has shown also that pain usually persists after section of the posterior sensory root of the trigeminal nerve in postherpetic trigeminal neuralgia.

Grantham[20] and Peyton and French[21] were the first to revive the skin excision method of treating chronic zosterian neuralgia. Since then Browder[22] has also reported four cases of postherpetic neuralgia treated by excision of the skin. Upon hearing of Grantham's cases, it occurred to us that wide elevation of skin flaps, going down to the muscle, might be a more efficient and practical manner of handling this problem, particularly when wide areas of skin are involved. It was also felt that a better denervation of the skin might be obtained and that, at the same time, one might accomplish not only a sensory denervation of the skin but possibly a superficial sympathectomy. Three cases reported here have given this method a trial.

REPORT OF CASES

Case 1.—A 68 year old farmer was first seen in October 1947. He had had typical acute herpes zoster in August 1947, over the right lower chest and abdomen in an area

corresponding approximately to the eighth, ninth and tenth thoracic dermatomes. He had received 42 days of osteopathic treatment, consisting chiefly of adjustments to the spine for the acute neuralgic pains. Vesicles had disappeared within about two weeks, leaving the typical hyperesthetic, somewhat erythematous skin, accompanied by severe postherpetic neuralgia in a wide band around the right side of the chest. The patient was treated subsequently with tetraethylammonium chloride, which was first given intravenously in doses of approximately 300 to 500 mg. At first the effect was dramatic, lasting from 48 to 72 hours. Gradually the effect seemed to wear off, and administration even at eight hour intervals resulted in only transitory and incomplete relief. The patient was then treated by paravertebral block, using Novocain, Metycaine, Intracaine in oil and Nupercaine in oil, and finally alcohol block, using absolute alcohol on the eighth, ninth and tenth roots. Each injection gave him relief from a few hours to two or three days. Alcohol gave the longest relief, lasting for approximately two weeks. He was then given x-ray therapy over the spine and sixth to tenth thoracic posterior root ganglia. This also gave transitory relief, and treatment was carried out over a period of approximately two and one-half to three months. Subsequently multiple paravertebral blocks were resorted to until April 1948, when a large skin flap comprising the involved herpetiform area was elevated. Immediately afterward the patient had complete relief from all pain. However, beginning three months following surgery there was some return of the deep burning sensation, but none of the superficial pain. Before surgery he could not endure bed covers or any clothing touching his skin. That has not bothered him since surgery. It is of interest that there is no sweating in the operated area and that the skin resistence remains high.

The psychic factor is well recognized in this patient, since he is worse whenever there is any difficulty at home. He was considering extensive thoracic sympathectomy, but on examination May 11, 1949 he stated he had no pain or burning, was sleeping without a sedative and felt fine. He had also solved certain family problems. As late as March 1951 he was still completely free of pain.

Case 2.—A 68 year old white man was first seen in May 1948, because of postherpetic neuralgia of the left thorax which had been present since January 1946. He had had typical herpes zoster involving the skin over the left upper thorax and the inner aspect of the left arm down to the elbow. He had been swathed in cotton for three months because of the pain, but he continued to complain of a burning, painful paresthesia over the involved area. He had received the usual therapeutic measures, including thiamine chloride, B complex, multiple vitamins, liver extract, intravenous tetraethylammonium chloride and paravertebral and intercostal nerve blocks, all without benefit. Otherwise his past history was not contributory. It was of interest that emotionally he had always been a very stable individual.

Examination disclosed an elderly white male who appeared to be in chronic discomfort. The general physical and neurologic examinations were not remarkable aside from the herpetiform scars in the skin involving almost the entire left chest from the posterior midline almost to the anterior midline. The second to fifth thoracic dermatomes were involved.

Denervation of the skin area was carried out, utilizing a very large skin flap, based caudally, so that the entire involved skin area was elevated from the chest wall down to the muscles and immediately sutured back in place and pressure bandage applied. The patient made an uneventful postoperative recovery and had relief from all pain until April 1950. However, when last examined in March 1951, there was

considerable return of sensory function throughout the entire affected area with some mild return of postherpetic neuralgia.

Fortunately in this case two pieces of nerve tissue were saved for microscopic study which revealed nerves embedded in fatty tissue showing evidence of some vacuolization of the myelin sheath, thus giving evidence of degenerative change in the distal portion of these particular intercostal nerves.

Case 3.—A 63 year old white woman had herpes zoster on the left chest in June 1948. The vesicles healed rapidly in five or six days, but she had almost constant pain and pruritic paresthesias over the left seventh to ninth thoracic dermatomes. Past history disclosed that she had been chronically ill for 40 years, most of which appeared to have been neurotic in nature. She had a nervous breakdown at age 33 after the birth of her fifth sibling. Following this she did not walk for seven years. She had had short relapses about every six months.

Examination made on December 23, 1948 disclosed irregular, patchy, depigmented scars over the left chest, anteriorly and laterally (very few posteriorly) over the above mentioned dermatomes. Light touch in the affected area was said to aggravate the burning and itching. Pinprick was described as dull, burning and an ache. The rest of the physical examination was not remarkable. Neurologic examination gave no evidence of any alteration of function in the central nervous system such as might have caused the inability to walk for 7 years.

On December 29, 1948, a large skin flap was raised (figures 1 and 2). It was elevated down to the muscles from above downward, remaining attached caudally. Closure was then effected by replacing the flap and suturing it in place with silk. Two Penrose drains were placed in the lower portion of the wound and a pressure dressing applied.

The patient recovered rapidly from the operation and admitted she was without pain. About ten days or two weeks postoperatively she began to complain of some deep burning, but this was not severe. When it was suggested that another operation (extensive thoracic sympathectomy) might give her relief, she decided the burning was not severe enough. She has been very well until the present time without any skin burning. At three months postoperatively the skin area was still anesthetic and anhidrotic. One year after surgery she still showed marked relief from pain although she complained of some distress.

COMMENT

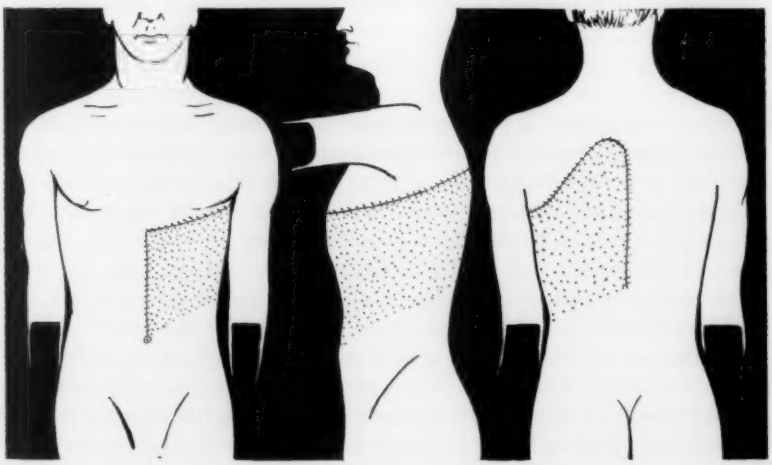
It is apparent that excellent results have been obtained in two patients and fair to good results in one other patient with postherpetic neuralgia involving the thoracic spinal nerves. In one patient (case 3) where there were strong psychogenic factors, mild to moderate deep burning pain still persists.

DISCUSSION

The pathology of herpes zoster has been reviewed extensively, beginning with the work of Haight[28] who showed that the peripheral nerves were involved. This was followed in 1861 by Bärsprung[23] who believed that the posterior root ganglia were the site of the disease. Finally its

FIG. 1. (left) Photograph of skin flap elevated from below upward (Case 3).

FIG. 2. (below) Diagram disclosing skin area elevated. Incisions were made in the midline, anteriorly and posteriorly, and connected along the caudal border of the area to be elevated down to the muscles.



pathology was definitely established by Head and Campbell[24] in 1900, who showed that not only were the peripheral nerves, posterior root ganglia and posterior roots involved, but also the posterior column in the spinal cord. Because of the involvement of the spinal cord, Head and Campbell suggested that this condition might be designated as a "posterior poliomyelitis." Confirmation of the cord involvement has been made by various others since that time. Hassin[29] quoted Bielschowsky as also having found changes in the sympathetic ganglia, thus making it most difficult, from the pathologic standpoint, to determine the exact origin of the pain. As Grinker[16] says, "If the disease were a pure ganglionitis, postherpetic pain should theoretically be alleviated by post-ganglion neurectomy. More often than not, the pain is not relieved by cutting the radicular nerve or injecting alcohol into the ganglion. The pain therefore probably represents a central irritative process in the posterior gray columns of the cord or sensory medullary nuclei." To this might also be added the possibility that the pain may be mediated through sympathetic nerve fibers and tracts, which might well explain why denervation of the skin by elevation of skin flaps, removal of the skin or limited posterior root rhizotomy give partial but not complete relief from symptoms.

Evidence that sympathetic fibers may play a role in transmission or production of this pain in relation to zosterian development of the ophthalmic division of the trigeminal nerve was brought out by Hyndman.[10] He states, "So far as I am aware, no one has expressed the idea that postherpetic neuralgia (ophthalmicus) is mediated by afferent sympathetic fibers and hence may be eliminated by removal of the stellate and upper 2 or 3 thoracic ganglia." Following Hyndman's suggestion two patients with ophthalmic postherpetic neuralgia were treated by upper dorsal sympathectomy. These patients had previously had peripheral alcohol nerve block, posterior sensory root rhizotomy of the gasserian ganglion and greater superficial petrosal neurectomy performed without relief. Likewise, prolonged intravenous therapy with tetraethylammonium chloride gave only slight and transitory relief. These two patients obtained only temporary relief following removal of the upper thoracic sympathetic ganglia by means of an anterolateral approach. Our experience, therefore, has not confirmed Hyndman's suggestion in regard to upper dorsal sympathectomy for postherpetic trigeminal neuralgia and suggests that the pain in these cases is not mediated through the upper dorsal sympathetics nor is the greater superficial petrosal nerve involved in the mediation of the pain. However, the spinal nerve involvement in postherpetic pain may not be the same as that found in trigeminal postherpetic pain. This is further suggested by the now recognized fact that

most patients with acute herpes zoster obtain temporary relief from pain with procaine sympathetic nerve blocks; likewise, sympatholytic drugs such as tetraethylammonium chloride frequently give temporary relief from pain. Whether or not the pain in acute herpes zoster is caused by vasospasm, as suggested by Findley and Patzer,[6] is problematic but it seems doubtful that postherpetic neuralgia would be entirely on this basis. Nevertheless, we have found autonomic blocking to give relief in many cases of postherpetic pain. Just why this occurs will certainly need further investigation but does suggest that autonomic fibers are affected.

Our inquiry into the autonomic aspect of the mediation of pain in postherpetic neuralgia is brought about because we have repeatedly been disappointed in the value of posterior root rhizotomy as well as intercostal neurectomy. Our experience with the elevation of large skin flaps, that is, elevating the entire area of skin and subcutaneous tissue involved in the postherpetic neuralgia, has given prolonged relief. In looking for reasons for this, it has appeared to us that in elevating the skin we have performed not only a sensory denervation but also a sympathetic denervation of the involved area, and it may be the combination of these two factors which has brought satisfactory results. It may be that extensive thoracolumbar sympathectomy (T3 to L3) together with multiple neurectomies rhizotomies by means of thoracotomy will be the only answer to perplexing problems such as may be arising in case 2 reported here. We favor the lesser procedure, that of the elevation of skin flap, in all cases of persistent postherpetic neuralgia. Only when this fails to give relief should one consider the more extensive surgery of sympathectomy combined with multiple neurectomies.

SUMMARY

Three patients with postherpetic neuralgia of the trunk were treated by elevation of the skin down to the muscles over the entire involved area (skin flaps, based caudally). Excellent relief from the burning pain was achieved in two patients and fair to good results in the third. In one case there has been some return of postherpetic neuralgia one and one-half years later.

It has been stated that in elevating the skin and subcutaneous tissues one is performing not only a deep subcutaneous sensory denervation of the skin but also a peripheral (subcutaneous) sympathectomy. It is suggested that postherpetic pain may, in part, be mediated through sympathetic (autonomic) fibers.

For the relief of postherpetic neuralgia elevation of the involved skin from underlying muscles, following the dermatome patterns, is suggested

as the operation of choice, particularly in debilitated patients. However, if failure is encountered or if the pain returns later, then extensive sympathectomy with rhizotomy or intercostal neurectomies is to be considered.

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Alterations of Cerebral Functions in Pheochromocytoma

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Reports of tumors arising from chromaffin tissue of the adrenal gland (pheochromocytoma) and from ganglia of the sympathetic nervous system (paraganglioma) are being reported with increasing frequency (table 1).[1-8] The pressor substances[9-13] from these structures discharged into the general circulation produce effects that are of special interest to the neurologist and psychiatrist. The clinical picture resembles that of anxiety states, vasovagal attacks and hypothalmic disorders. The syndrome consists of paroxysmal or sustained hypertension, palpitation, sweating, pallor, tremulousness, headache, dyspnea, nausea and vomiting, pain in the precordium and epigastrium and muscular weakness. Also encountered

TABLE 1
Cases of Pheochromocytoma Reported in the Literature

Author	*Year*	*Cases Collected*
Biebl and Wichels	1925	14
Rabin	1929	30
Belt and Powell	1934	60
Brunschwig and Humphreys	1939	103
Kirschbaum and Balkin	1942	116
MacKeith	1944	165
Calkins and Howard	1947	176
Davis, Hull and Vardell	1950	203

are vasomotor phenomena such as discoloration of the hands and legs or blanching of digits, as well as hypermetabolism, glycosuria, amenorrhea, changes in urinary frequency, loss of libido and hyperthermia.

These findings raise many problems in differential diagnosis despite

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assistance obtainable from clinical tests with benzodioxane,[14] histamine[15] and the tetraethylammonium ion.[16] Paroxysmal hypertension, a prominent feature in most cases, also occurs in tabes dorsalis,[17, 18] lead poisoning,[19] thalamic tumor,[20] carcinomatous involvement of the vagus,[19, 21] meningitis,[22] affections of the gasserian ganglia,[23] sciatic neuritis[24] and spinal cord injuries.[25] When the tumor effects persist, hypertensive changes lead to alterations of the cerebral blood vessels so that neurologic and psychiatric complications often supervene (table 2).[1, 2, 5, 26-48]

TABLE 2

NEUROLOGIC AND PSYCHIATRIC COMPLICATIONS OF PHEOCHROMOCYTOMA

Author	*Year*	*Sex*	*Age*	*Neurological Complications or Findings*
Sloan, Schlesinger	1950	M	23	Massive cortical and subcortical hemorrhage
Hatch, Richards, Spiegl	1949	M	23	Hemorrhage into pons, cerebral peduncle and IV Vent.
Manlove	1949	M	54	Multiple hemorrhages and scarring in brain
Spatt and Grayzel	1948	F	51	Metastatic lesions to brain
	1948	F	34	Left hemiparesis
	1948	M	54	Intracerebral hemorrhage
Brunschwig	1947	F	39	Left hemiplegia
Fontaine, Warter, Wilhelm	1947	M	33	Absent abdominal reflexes on side of tumor
Mortell, White	1945	M	49	Convulsions
Koster	1945	F	34	Subarachnoid hemorrhage
Waller	1945	M	49	Cerebellar hemorrhage, subarachnoid bleeding
Dolgin	1945	M	24	Death following minor head trauma
Menscher	1944	F	23	Reflex changes
Linneweh	1942	M	10	Convulsions, generalized arteriosclerosis
Strickler	1942	M	32	Meningeal signs
Kirschbaum, Balkin	1942	M	53	Massive cerebellar hemorrhage
Knake	1942	M	11	Atherosclerosis of cerebral vessels
McGavack, Benjamin, Speer, Klotz	1942	F	43	Metastases to vertebral column
Philips	1940	M	39	Hemiplegia at 33; Horner's syndrome
Kremer	1936	F	14	Left cerebral thrombosis, int. hydrocephalus
Hick	1933	F	64	Ruptured aneurysm of ant. communicating artery
Barker	1930	M	47	Multiple vascular lesions of brain
Labbe, Azerade, Violle	1929	M	29	Cerebral hemorrhage
Rabin	1929	F	45	Meningeal signs, coma; no brain findings
Zeckwer	1925	F	36	Softening right internal capsule, aortic syphilis
Biebl, Wichels	1925	M	36	Old and fresh intracerebral bleeding
von Neusser	1910	F	25	Brain hemorrhage
Wiesel	1909	F	2½	Cerebral arteriosclerosis

Our interest in pheochromocytoma arose during combined medical, experimental psychological, neurologic and psychiatric studies on patients with essential hypertension. Evidence has been presented that impairment of cerebral functions may take place early in the course of essential hypertension.[49, 50] The techniques employed in these studies have been described elsewhere.[51, 52, 53]

CASE REPORT

A white girl aged 14 entered the clinic on December 9, 1948, complaining of episodes of dyspnea, recurrent headaches, failing vision, palpitation, weakness and loss of weight over a period of one year. A month previously, two weeks after the death of her mother, an attack of dyspnea and palpitation was of sufficient intensity to require emergency treatment by a municipal pulmotor squad.

Physical examination:—The patient was slender and moderately hirsute. The optic discs were blurred; there was retinal edema with marked localized arteriolar constriction. The heart was enlarged to the left, and there was a soft systolic apical murmur. The kidneys were palpable through the thin abdominal wall. Blood pressure was 250/160. The neurological examination was normal.

Laboratory data:—The standard urea clearance was 50 per cent of the mean normal value. The three hour glucose tolerance curve was diabetic. Metabolic rates varied from +20 per cent to +41 per cent. The heart was 25 per cent oversized as measured by the frontal plane area. Skull x-rays and intravenous pyelograms were normal. 16 mg. of benzodioxane given intravenously caused a precipitous drop in blood pressure. Serial electrocardiograms showed abnormalities of a nonspecific type. Cardiac output, estimated by the low frequency critically damped ballistocardiograph, was seven liters per minute. The preoperative period was characterized by sustained hypertension and rapidly failing vision. Numerous flame-shaped hemorrhages appeared in the retinas, the optic discs became elevated and the blind spot enlarged; the patient was unable to read.

The history, clinical findings and response to benzodioxane were highly suggestive of pheochromocytoma. On December 20, 1948, a spherical pheochromocytoma measuring 3.5 cm. in diameter was removed from the region of the right adrenal gland. The blood pressure fell to normal limits immediately on clamping the pedicle of the tumor. Except for a rapid pulse rate, the patient's postoperative course was uncomplicated. The responses to histamine, benzodioxane and tetraethylammonium chloride, as well as tolerance to glucose, were normal a few days following the operation and six months later. In July 1949 the electrocardiogram, ballistocardiogram and visual fields were within normal limits. At that time, the blood urea clearance was 90 per cent of the mean normal value.

Psychiatric examination:—The patient was a shy adolescent who responded politely but never spontaneously in the daily preoperative interviews. Her stoical attitude was reflected in the dispassionate account of her illness and in her ready compliance to numerous laboratory tests. She complained of poor vision and headache. Although pallid and perspiring profusely, she sat quietly. She did not describe a feeling of impending doom during the recurrent episodes of palpitation, dizziness, dyspnea, headache and weakness. She recalled that she was uncomfortable during the acute attack of dyspnea and palpitation which prompted her sister to call for a pulmotor squad. She had not been apprehensive.

The youngest of five siblings, the patient was born 13 years after the fourth child and 23 years later than her oldest brother. Her father, an immigrant laborer, died of a stroke when she was five. The mother, an invalid for many years, died of high blood pressure and diabetes. The patient stressed her ability to care for herself. She planned to graduate from high school so that she could become self sufficient. She recognized, however, that she had not been able to concentrate on her studies since January 1948, when she became excessively tired, slept much and lost weight despite a good appetite.

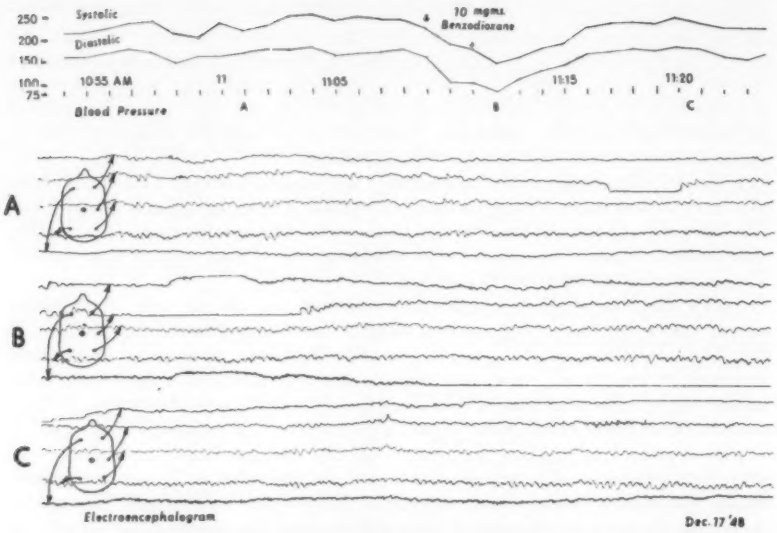

FIG. 1. Mild irregularities in all areas; a few waves are slower than the alpha rate of 8 per second. Benzodioxane reduced blood pressure to normal limits for approximately 4 minutes; no appreciable change in tracings B. At C blood pressure has returned to level of A.

She had also abandoned recreational activities which consisted of bicycling, roller-skating and walking with girl friends. She disavowed interest in boys and only reluctantly mentioned irregularities in her menstrual cycle during the past half year. She admitted some memory lapses since the onset of illness; they had increased noticeably during the previous month. She had grieved over her mother's death, but displayed no special preoccupations indicative of depression.

Repeated psychiatric examinations provided evidence of mild characterological difficulties in an emotionally inhibited adolescent of average intelligence. Her major ego defenses were designed to deny feelings of dependency and allay fears of abandonment.

The patient asked permission to return to school during the second week of February 1949. On February 19 shyness and reserve were still prominent. She reported casually that her menses had become regular, and expressed the hope that she would soon be able to join her girl friends in athletic activities. She said: "I can remember things better. There's lots of things I can remember now." This statement not only attested to the return of her memory but was also designed to communicate feelings of anxiety while discussing personal matters.

Performances in the psychology laboratory:—The patient was examined on December 15 and 17, 1948. Decreased visual acuity made it necessary to omit a verbal

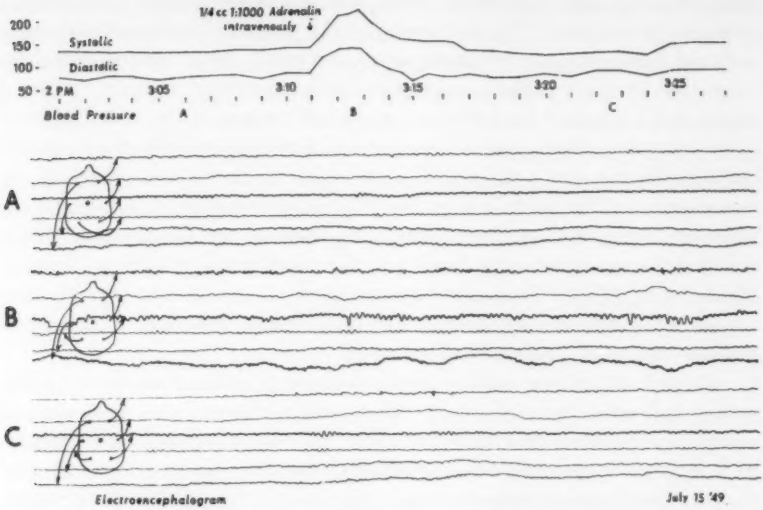

FIG. 2. Seven months postoperatively, the tracings are more nearly normal. A 4 minute elevation of blood pressure by adrenalin B induces a slight increase in irregular activity in all leads. At C blood pressure has fallen to level at A.

test. She rated a performance I.Q. of 67, which was regarded as a remarkably suppressed score. Where items were printed in large type, the patient attained normal scores on personality tests. Impairments of the A factor (abstraction) and the P factor (power) were observed. In spite of normal performance in the control tests evaluating biological intelligence, the impairment index[53] was .7. This value indicates impairment of frontal lobe functions.

On reexamination April 30, 1949, an estimate was made of the power factor and other tests in the battery that were relatively free from learning effect. The extrapolated impairment index was .8.

The patient was retested July 14, 1949, and the performance I.Q. was 102, the verbal I.Q. 86. However, the impairment index was .2, a value compatible with performances of the control group. Both quantitatively and qualitatively, the performance of this girl revealed a marked reorganization of adaptive capacities. This is manifested in her ability to handle abstraction and the good to superior power factor.

Electroencephalographic studies are summarized in figures 1 and 2.

DISCUSSION

Cerebral vascular disorders are common in unrecognized chromaffin tissue tumors. Wiesel[48] found generalized arteriosclerosis in a two and one-

half year old girl. Linneweh's ten year old male subject had similar vascular alterations.[37] The average age of 15 patients who developed intracerebral hemorrhage or thrombosis was 36 years. Mild trauma is poorly tolerated. Dolgin's patient, a 24 year old soldier, died four days after a minor head injury.[35] In addition to a small tumor in the right adrenal, there were only dilatation and congestion of all cerebral blood vessels and their capillaries and a 0.5 cm. by 0.5 cm. ecchymotic area over the inferior aspect of the right frontal lobe. Rabin[2] encountered meningeal signs followed by coma which he attributed to necrosis and hemorrhage within the tumor since neither the brain nor the meninges showed any changes. Mortell and Whittle[32] reported a recurrence of convulsive attacks after a five year symptom free interval. The exacerbation coincided with clinical manifestations of a pheochromocytoma.

Clinical experience with patients following surgical removal of the tumor indicates, however, that the vascular changes are reversible in many. Several observers have described the return of the blood pressure to a normal range following successful operative intervention. One of the most striking examples is that of Spear and Griswold[54] who reported the case of a 51 year old woman with typical symptoms for 21 years and a preoperative blood pressure level of 250/150. Bruce[55] reviewed findings in the ocular fundus in patients with pheochromocytoma. He described the preoperative and postoperative ophthalmologic findings in two patients. Changes such as retinal hemorrhage, exudate, papilledema and denting of the veins may regress or even disappear following extirpation of the tumor. These observations lend support to the concept that, under certain circumstances, severe vascular alterations may be reversible.

Electroencephalographic studies have been reported previously. Raab and Smithwick[56] and Spatt and Grayzel[29] observed essentially normal records. Guarneri and Evans[57] noticed a "definitely atypical record consistent with mild form of epileptic dysrhythmia with no localized abnormality" in a 23 year old woman. Bruce recorded the electroencephalographic report of an 11 year old boy.[55] There were "bursts of high voltage, 3 second activity seen synchronous in all leads and transient right parietal focal signs." In the patient mentioned previously, Mortell and Whittle wrote that "the tracing in general showed more slow activity than in the normal person of this age."[32]

Psychiatric reactions have been described in few of the reports. The patient of Vaquez, Donzelot, and Geraudel[58] and Hahn[59] exhibited toxic-delirious reactions. The 11 year old boy reported by Snyder and Vick[60] entered into a short manic episode when perirenal insufflation was done in an effort to establish the diagnosis. Barker's patient was delu-

sional and hallucinatory and was found to have multiple cerebral hemorrhages.[44] Perkins, in a personal communication to Bruce, observed a similar reaction.[55] Spaulding[61] reported loss of consciousness in five patients. Occasionally loss of libido is encountered.

Of special importance and interest are the phenomenologic differences between the adrenal-sympathetic crises in pheochromocytoma and similar symptoms in anxiety states and vasovagal attacks. Gowers was careful to point out in his original description of vasovagal attacks as an epileptic variants that a sense of impending doom or a fear of death is an important part of the disorder. Similarly, the feeling of apprehensiveness is an important aspect of the anxiety syndrome. A sensation of impending doom or imminent danger is rarely described in association with pheochromocytoma. In the two patients that we have had the opportunity to observe, it was not present. The paucity of affective response in the presence of somatic concomitants of anxiety recalls to mind the experimental studies of Bard[62] on the mechanisms of sham-rage and the clinical experience with patients with severe cortical damage. Bard's animals manifested all the physiologic signs of intense emotional arousal characteristic of rage without, of course, definitive evidence of any subjective accompaniment. Presumptive evidence of its absence, however, is revealed by the rapid extinction of the signs upon withdrawal of stimulation. Severe cortically damaged patients seem to be capable of most components of anxiety except the elaboration of the sensation of fear or impending danger. This disassociation of effect was also observed by us in patients with brucellosis and diabetes,[63] in whom other evidence of cerebral involvement was obtained. It is suggested, therefore, that the disassociation of effect observable in most patients with pheochromocytoma be attributed to temporary circulatory disturbances of the brain with disassociation of the neural elements involved at the highest levels of integration.

Kasanin's[64] psychiatric study of a 31 year old woman who was relieved of symptoms after surgical removal of a pheochromocytoma is pertinent. He reported that the patient "often had a peculiar sensation in her heart which throbbed and beat rapidly, making her feel very uncomfortable. She compared this sensation with the feeling of inward excitement one gets from a serious emotional situation, except that these feelings are not provoked by any external stimulus. It was like an emotion without reason."

CONCLUSIONS

1. The neurologic, psychiatric and electroencephalographic aspects of pheochromocytoma are reviewed.

2. Combined medical, neurologic, experimental psychologic, electroencephalographic and psychiatric studies, done preoperatively and postoperatively on a 14 year old patient with pheochromocytoma, reveal that temporary impairment of cerebral cortical functions takes place. The generalized systemic vascular changes are accompanied by similar alterations in the cerebral blood vessels and are reversible.

3. It is suggested that the somatic experience of anxiety is disassociated from consciousness by virtue of temporary cerebral cortical dysfunction.

4. Preoperative and postoperative electroencephalographic readings showing the effects of benzodioxane and adrenalin on the tracings are recorded.

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• I hope the reader of these observations will endeavor to divest himself of all prejudices upon the subject, and examine, one by one, and with rigid impartiality the various methods which have been recommended by writers, to determine what are the functions of the brain. Such an examination seems to be necessary at the outset, that we may ascertain satisfactorily to ourselves, which of the methods proposed will be most profitable for us to pursue.

We should also call to mind that but little is now known upon this subject; that all physiologists of reputation and candor admit, that though no other subject is more deserving of thorough investigation, yet there has been but a small amount of evidence furnished, to enable us to determine with accuracy the office, or use, of the various parts of the brain of man. It therefore devolves upon the anatomists, physiologists and pathologists of the present generation, to make investigations upon this important subject to a far greater extent than have hitherto been made, in order to dispel the darkness, in which it is at present involved.

—Amariah Brigham in *An Inquiry concerning the Diseases and Functions of the Brain, the Spinal Cord and the Nerves*, published in 1840.

Electroencephalographic Findings in Post-Traumatic Encephalopathy

Andre A. Weil, M.D.

THIS is a report of electroencephalographic findings in 50 patients who suffered from what is commonly called "post-traumatic encephalopathy." Included are cases which were examined because of late effects and sequelae following cerebral injury during a six months' period. The etiology covers a wide variety of cranial traumas ranging from simple prolonged post-concussion syndrome to open and closed focal injuries to the brain, residuals of penetrating injuries and simple and comminuted fractures. Recent acute brain injuries were excluded. In spite of the variety of injuries, certain clinical features were common in all case histories, namely headache, dizziness (especially on change of posture)*, psychomotor fatigue, frequent disturbances of the equilibrium and forgetfulness. These symptoms, loosely connected as they may appear to be, have been grouped under the general heading of post-traumatic encephalopathy. Clinically, differentiation between patients can be made in three entities, the borders of which are fluent and frequently overlap:[1] (1) the post-concussion syndrome, apparently due to disturbed vasomotor balance and certain disorganization of the finer structures of the brain; (2) focal injuries to the brain; (3) cases which showed no neurologic findings and where the patient's attitude toward the injury and his desire to recover played the decisive role. The last group has been frequently thought to have no demonstrable neurophysiologic findings. The present investigation, as well as those of others, have proved the opposite, however.[2]

A review of the literature on the subject reveals that excellent and adequate work has been done as to the value of the electroencephalogram in brain injuries, particularly in cases with severe organic traumas. Jasper and co-workers found that in 31 post-traumatic cases whose complaints "consisted chiefly of headache, dizziness, and nausea" approximately 85

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per cent had cortical dysrhythmias.[3] Laufer and Perkins[4] found among their 159 patients 20 per cent with marked electroencephalographic abnormalities, 8.8 per cent with focal records and 36.7 per cent with striking incidences of hemisphere and amplitude asymmetry. The degree of electroencephalographic abnormalities increased from closed to open cases. The longer the interval between injury and electroencephalogram, the less was the incidence of abnormality. Severe head injuries presented the greater portion of abnormalities and focal records. On the other hand, reports by Puech and co-workers[5] indicate that even recent injuries can produce nearly normal electroencephalograms and that recent fractures, concussions or even lacerations of the brain may cause only slight abnormalities. They concluded that a normal electroencephalogram cannot definitely rule out post-traumatic cerebral lesions, and recommended that in such cases repeated recordings should be made from many areas.

It was noticed very early in the present investigation that "post-traumatic encephalopathy" was too loose a clinical syndrome to be lumped together for electroencephalographic purposes. Therefore, the 50 patients were classified in two groups: Group A—those without significant neurologic abnormalities; Group B—those with neurologic abnormalities or with manifest epilepsy arising at least two years after trauma. Twenty-seven cases were classified under group A and 23 fell under group B. When the results were compiled, electroencephalograms were classed according to normal, questionable, pathologic and grossly pathologic, using a method previously described.[6]

A glance at figure 1 shows that group A is almost a mirror image of group B. For instance, 37 per cent of the cases without significant neurologic abnormalities had a normal electroencephalogram, whereas none of the cases in group B had a normal pattern. Taking the other end of the scale, only 19 per cent, the smallest group in A, showed grossly pathologic records, whereas 48 per cent, the largest group in B, showed grossly pathologic patterns. In trying to classify the records according to focal and diffuse irregularities, even more striking discrepancy between groups A and B was noticed. Group A showed only 22 per cent focal irregularities whereas 78 per cent were diffuse. Exactly the opposite was true for the group with neurologic abnormalities where 83 per cent had focal irregularities and 17 per cent were diffuse. Considering clinical correlations, it should be noted that the majority of normal electroencephalograms and questionable electroencephalograms in group A consisted of cases where the concussion or fracture had occurred more than one year previously. More than half of these cases had compensation claims pending, and the volume and frequency of complaints seemed to increase with examina-

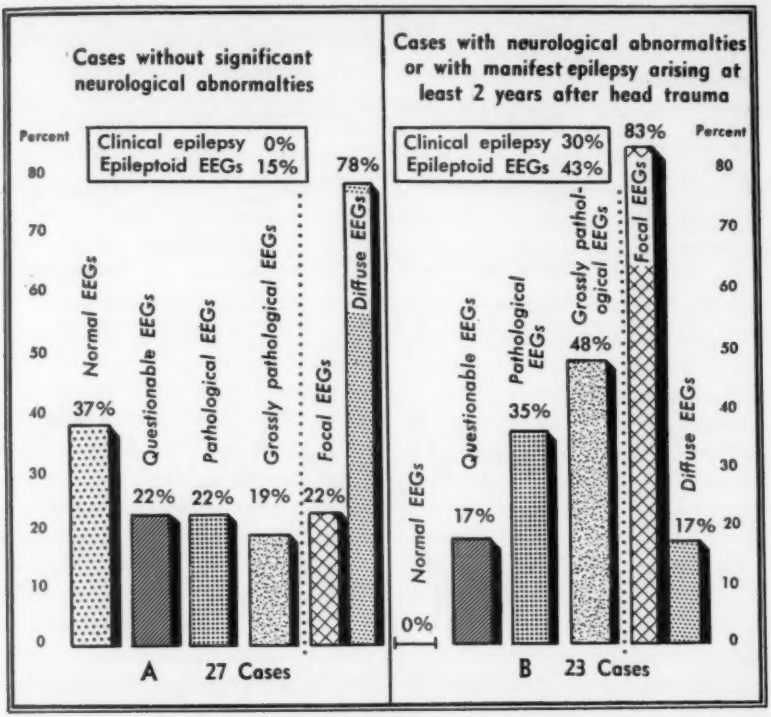

FIG. 1

tions. It was also noticed that the grossly pathologic electroencephalograms in group A consisted of cases with severe concussions or fractures which preceded the electroencephalogram by a period of months, even though the neurologic examination showed no significant abnormalities. The majority of grossly pathologic records in group B consisted of patients where open skull injury had occurred. In both groups the patients of younger age, particularly those under 20 years old, showed more pronounced abnormalities in the electroencephalogram than the older patients.

Without going into the detail of the problem of post-traumatic epilepsy, it should be mentioned that the figures presented here do not show the true incidence of this disorder in the average population, since many of the cases were referred because of convulsive manifestations and not because of the original head injury. This may explain the high incidence of 30 per cent of clinically manifest post-traumatic epilepsy in group B.

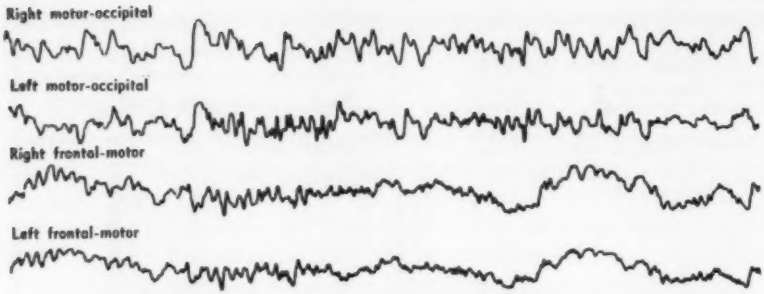

FIG. 2. A 30 year old female. Concussion August 13, 1948; EEG Sept. 7, 1948. 4 to 6 per second random slow activity of moderate voltage, random spikiness and 22 per second fast bursts. Tracing shows predominance over the right motor and temporal areas.

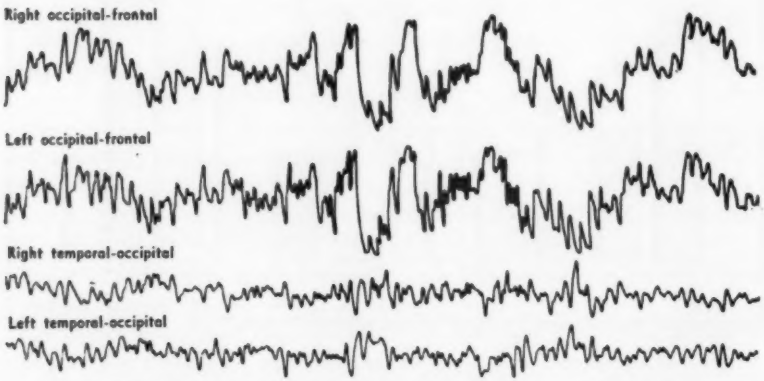

FIG. 3. A 37 year old male. Severe concussion on October 5, 1948; EEG October 19, 1948. Genuine high voltage random slow activity bifrontally; considerable change of pace and spikiness in the alpha and intermediate frequencies; no definite neurological findings at the time of the EEG.

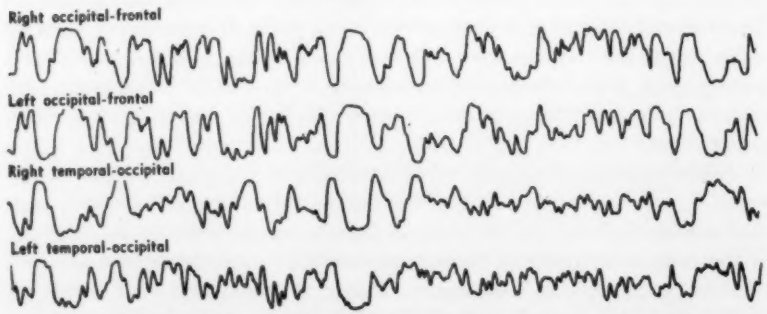

FIG. 4. A 24 year old male. Blast injury 1944; EEG Sept. 13, 1948. Immediate breakdown during hyperventilation, with synchronous epileptiform discharges. No definite history of epilepsy.

The most characteristic feature found in both groups was disorganization of alpha pattern with random 4 to 7 per second slow waves of moderate voltage interspersed. Fast bursts up to 50 mV were also fairly characteristic as were random monophasic and biphasic spikes and sharp waves (figure 2). The fast activity and spiky activity was particularly noticeable in the anterior leads which are comparable to the phylogenetically younger portion of the cortex (figure 3). The cases with epileptoid patterns showed, of course, typical dysrhythmic paroxysms, usually more dissociated and less regular than in the idopathic type of epilepsy (figure 4).

Focal abnormalities consisted mainly of voltage depression, which was in all probability the neuropathologic equivalent for gliosis over specific brain areas and of traumatic spiking over isolated areas. To the clinician group A is the more important one. Here we have patients with characteristic subjective complaints of post-traumatic encephalopathy with no significant neurologic or laboratory findings. The electroencephalogram may be of some help in differentiating the conversion hysterias and malingerers from cases with actual organic pathology. Even though 59 per cent of electroencephalographic records of Group A were normal or borderline, 41 per cent showed pathologic or grossly pathologic tracings, which indicates that not all their complaints were due to neurotic or similar trends. From a neurophysiologic viewpoint these records demonstrate the presence of depolarization of unit discharges, and the spiky fast activity in these records is highly indicative clinically of vascular damage. The question which comes up, of course, at the end of the consideration is a fundamental one, namely: What would the electroencephalogram have shown prior to the head injury?

SUMMARY

Electroencephalographic tracings of 50 patients with post-traumatic encephalopathy were correlated with their clinical findings. It was noticed that (1) the abnormality of electroencephalograms increased with the severity of trauma; (2) there was a definite increase of abnormal electroencephalograms (83 per cent) in patients who retained neurologic abnormalities; (3) there was a significant increase of focal electroencephalographic abnormalities (83 per cent) in patients of the latter group; (4) 41 per cent of patients without neurologic abnormalities showed irregularities of the electroencephalogram indicative of organic pathology. The importance of electroencephalography in malingering and post-traumatic epilepsy is discussed.

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• Everyone knows that certain symptoms indicate disease of the brain, or its membranes, or nerves; but until quite recently, and now almost generally, physicians rest satisfied with merely knowing that the disease is located somewhere within the skull. But we should certainly strive to know more about this, and I feel confident that by numerous and careful observations we may be able to determine from the symptoms, not merely that the disease is within the skull, but whether the membranes, or nerves, or the substance of the brain is affected, and often what part of this latter organ and what nerves are diseased. Few physicians are now satisfied with merely knowing that a patient has some disease within the abdomen or thorax; they seek to know what particular organ is affected, and what tissue or portion of the organ is diseased, and this knowledge they can generally obtain by a thorough examination of the case, and comparing the symptoms manifested with those exhibited by others where examination after death revealed the connection between the symptoms and the organic disease. But much of this knowledge—of this ability to determine the exact location of the disease within the abdomen, or chest—is of modern origin; and we have but to pursue the same course as regards diseases of the nervous system, in order to judge from the symptoms what portion of it is affected. This field of investigation is indeed very great, and will require for a long time many laborers, but ultimately, I apprehend, will richly reward those who cultivate it.

—Amariah Brigham in *An Inquiry concerning the Diseases and Functions of the Brain, the Spinal Cord and the Nerves,* published in 1840.

Intravenous Sodium Amytal in Generalized Language Dysfunction

George N. Raines, M.D. and Robert Cohn, M.D.

In the study of language function disturbance resulting from relatively focal vascular lesions of the brain, it has been observed that, despite the focal nature of the primary lesions as recognized at autopsy, a general dissolution of language function is not uncommon. The recognition of such phenomena probably inspired von Monakow[1] to the idea of "diaschisis": the central idea of this concept was that when a major integrating element in a mutually interacting system became malfunctioning, the whole system underwent reorientation, and, in general, the reoriented system sustained a reduction in overall efficiency which was greater than might be expected if each element had equal weight in the total final output. von Monakow thus recognized the interdependency of parts of the brain for the total function necessary for interpersonal communication through symbols. He also demonstrated a deep understanding of the nonadditive aspects of the elements of language function. The von Monakow concept implicitly assumed that in language function, although only one mode may be employed in a given situation, expressive or receptive activity required a constant interplay of all euphasic elements. Any breakdown in generalized symbolic adaptation must then be followed by dysphasic activity of varied intensity in all spheres.

Contrary to von Monakow's idea is the concept embodied in the works of Pötzl,[2] Henschen[3] and Nielsen.[4] They believed that there was punctate localization for each of the elements of symbolic communication. Although they were quite aware of the interdependency of one mode of communication on all other modes, overtly unused in a given moment of interpersonal symbolic orientation, nevertheless they designated areas for the revisualization of animate objects, areas for calculation ability, areas for the appreciation of music and so on. Such a concept, in terms of what is observed in the great majority of dysphasic patients,

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merely implies that the most obvious superficial defects were under study, and that gradations and more subtle elements of disturbed communication function were allowed to remain as background phenomena.

In the search for a mechanism whereby general effects may result from primary focal lesions, it was felt that a physiologic inhibition or active suppression might play a major role. The work of McCulloch[5] and his co-workers made such an hypothesis appear rational. This idea gained importance when Bucy[6] showed that cortical suppression areas, similar to those demonstrated to be present in experimental animals, were operative in man. Hence, as a working hypothesis, it was assumed that the dissolution of generalized language function following focal lesions of the brain was the consequence of uncontrolled suppressor activity on the remaining structurally intact areas of the brain which served in the role of symbolic expression.

In order to test this hypothesis, pharmacologic agents were used in an attempt to inactivate differentially the suppressor elements and thereby allow the residual intact language areas to function more adequately. For this purpose sodium Amytal and sodium Pentothal were slowly administered intravenously in varied doses. It was assumed that, since the suppressor areas were a more recently acquired brain mechanism, according to the concept of Hughlings Jackson,[7] they should be more susceptible to any agent capable of decreasing the general cerebral function. Observations made on three selected cases in testing the above hypothesis are presented here.

Case 1.—A white man aged 37 years was admitted to the U.S. Naval Hospital, Bethesda, Maryland, on June 13, 1945. A few hours prior to admission, the patient had staggered suddenly, vomited and become paralyzed on the right side. The major presenting difficulty on admission was an expressive dysphasia marked by naming difficulties, dysgraphia (kinetic-practic in origin), paraphasia and a right hemiplegia.

On examination, the patient appeared well nourished and well developed, and lay quietly in bed. There was sagging of the right lower face, with ptosis of the right eyelid. The tongue protruded to the right and the soft palate was flaccid on the right side. Extraocular movements showed loss of voluntary conjugate deviation of eyes to right; the pupils were equal and reacted to light and in convergence. Ophthalmoscopic examination showed no pathologic change. The patient transiently manifested a labiolingual dyspraxia. He was capable of initiating motions in the right leg, but did not move his right arm spontaneously at all. Weakness was greater in the hand than at the elbow or shoulder joints. There was increased muscle tone in the extremities of the right side. Deep tendon reflexes were hyperactive on the right, with sustained right patellar and ankle clonus. The right plantar response was flexor in type, with slight fanning of the toes. No other pathologic reflexes were elicited. The abdominal and cremasteric reflexes were present but less active on the right. No sensory deficits were elicited at any time.

Laboratory findings, including repeated blood cultures, electrocardiogram, electro-

encephalogram, blood sedimentation rate, spinal fluid chemistry and serology, and x-ray studies were all within normal limits.

A formal aphasia test revealed no ideational practic difficulties. Visual and auditory verbal and object gnostic functions were intact, as were the tactile and topognostic elements. Throughout, marked difficulty in recalling the names of common objects of the environment and in using nouns in spontaneous speech was observed. Speech was not fluent. In the push for words the patient often used malformed and improper symbols (paraphasia and jargon). He often recognized the mistakes and attempted to correct them. He was fairly well accomplished in reading, with an understanding of even moderately complex statements. Writing, spontaneous and to dictation, was entirely similar to the phonetic output. Copying was well executed in his own handwriting. Calculations were readily and accurately accomplished. He apparently recognized tunes but was unable to name them. At no time was the patient able to hum or sing any song. Aside from the intense constriction of the vocabulary, the Adam and Eve story was narrated creditably.

The somatic motor deficit, with minimal spasticity of the limbs, and sparing of the verbalization apparatus, pointed to a lesion of the deep, penetrating branches of the left middle cerebral artery. The intense naming difficulty indicated that the lesion also involved the angular gyrus speech zone, either directly, as part of the middle cerebral artery thrombosis, or through interruption of its connections. Since the presenting difficulty of name recall and verbalization were observed in the presence of a fairly well integrated brain function, this patient was given sodium Amytal to determine whether the amnestic aphasic difficulty could be influenced by minimal relative functional inactivation of the brain.

One tenth gram of the drug was administered in approximately two minutes. This resulted in a transient, but dramatic, almost complete cessation of all language function. Paraphasia and jargon output became dominant as recovery from the administration of sodium Amytal occurred. Recovery to the pre-injection level of function occurred in about 15 minutes.

Case 2.—A white man aged 48 years had an appointment on June 18, 1946 at 4 p.m. which he failed to keep. On arrival home at 6 p.m., he was greatly confused and unable to make known his wants. During the evening the patient was observed to stagger slightly when he walked, but there was no evidence of paralysis. On the following day the patient was still confused, although he could make himself understood moderately well. He was hospitalized at that time.

On admission it was determined that the patient had been a known hypertensive for nearly 20 years. Together with the obvious language dysfunction, a moderate right lower facial paresis was observed. Funduscopic examination was essentially negative. On gross confrontation tests a right homonymous hemianopsia was suspected. Sensory tests were carried out with difficulty, but no gross impairment was elicited. Coordinate activity to request was not accomplished, but no spontaneous dystaxia was recognized. The deep tendon reflexes were brisk but equal. No reflexes of pathologic import were elicited.

The electroencephalogram showed marked focal slow activity over the left parieto-occipital region. Careful perimetric examination showed only minimal, peripheral, "ring" scotomota, bilaterally. The spinal fluid had a pressure of 220 mm. of water, with normal dynamics. All other laboratory findings were within normal limits, except for a transient left bundle branch block disclosed by the electrocardiogram.

Language function test showed a pleasant, alert and affable patient. He was able to find his way to the examination room without difficulty. He indicated recognition of all the common objects of the environment, but he experienced great difficulty in naming certain of these objects. Occasionally, when shown a nickel he named the coin correctly; a moment later he was unable to say "nickel." He seldom used circumlocutions when he failed to find the word that symbolized the presented object. Color naming and matching were accomplished with only moderate difficulty; red and blue shading were sometimes confused in matching. He was able to read short sentences and abstract their meaning. In reading, as well as in the naming of objects, he often sounded out the word; for instance, in naming a ruler, he said "rurer," "no rure," and then "ruler." When the proper sounds were finally emitted, a gleam of satisfaction invariably spread over his entire face. In speaking and reading there was a strong tendency to perseveration. When measuring with a folding ruler he opened the rule as if he had never seen such an instrument before. Other instruments, such as scissors and pencil, were manipulated in an entirely appropriate way. He could draw a very creditable picture of a cat. There was no difficulty in recognizing the major theme of a complex picture. He was able to hum a tune and recognized musical scores. No right-left disorientation was elicited. Multiplication and division operations of small numbers were carried out well; large numbers (4283 x 87) were multiplied correctly, but the "carry-over" numbers were often added incorrectly, indicating difficulty in remembering the number to be added.

Spontaneous writing was simple. It contained misspellings and inversions, such as "guitf" for "gift." He later changed this to "guift." He did equally well with the eyes open or closed. Left handed writing was not superior to that of the right.

In copying script he wrote for "The Lord is my shepherd I shall not want," "The Lord is my Shepard I Lord is my S I shall not want."

To dictation, he wrote, "Our Farther h who art in heaver." He recognized his mistakes but was unable to correct them. Semantic defects were not clearly recognized. To the Adam and Eve story he said, "It is a fable." Following that he tried but could not muster sufficient words to say why it was a fable. He simply remained blocked.

Following this initial episode the patient spent long hours relearning to read and write, and regained a remarkable degree of function.

After a minor argument with his wife on the evening of February 2, 1947, the patient showed progressive confusion, blank facial expression and difficulty in speech. Shortly after going to bed, he developed a Jacksonian-like convulsion with rotation of his head to the right and clonic movements of the right arm. Following a fifteen minute interval of flaccidity, a similar attack of longer duration occurred. The patient was seen at home an hour and a half after the last convulsion. He was restless and aware of his surroundings, but showed obviously impaired ability to understand questions. He was returned to the hospital immediately. On readmission, aside from slightly more active right biceps and radial periosteal reflexes, no neurological abnormalities were observed. The pupils were round and equal, responded well to light and in convergence. The visual fields were believed full on gross testing.

The spinal fluid pressure at this time was 280 mm. of water. An electroencephalogram showed generalized slow activity, particularly over the left brain, with a maximum slow wave output over the left parieto-occipital region. On February 3, 1947, when the patient was brought to the examination room, he appeared somewhat bewildered. He greeted the examiner with, "Hello, Doctor, come on in." This was followed by an

incomprehensible mass of words that had only occasional relevancy. He apparently recognized no auditory, verbal or object symbols. Occasionally he read spontaneously a number such as 400 as "four" "zero" "zero," but more often read 2 × 2 as "z" "x" "z" and 7 as Y (the paraphasic element should be noted). "Comb" was never recognized by its verbal symbols, but a comb was immediately recognized when shown to him. Body imagery was at no time appreciated correctly. He repeated the word "nose" no less than twenty times with no overt recognition of it as a body part.

Spontaneous writing consisted of numbers. The written and verbalized number never corresponded. He wrote "cat" to dictation, but "table," after five attempts, was successively, "CA," "CAB," "CABL," "CALEH" and finally, "CAHACH." All testing of subtle language function was fruitless, as the requests to execute most operations were not comprehended completely. Mimicry was accomplished well at all times.

Within 24 hours following the above examination, the patient regained his language function precipitously to a degree approximating that observed prior to the most recent disturbance. The patient felt his word understanding, reading and speaking ability were 50 per cent better than before the last episode.

In this condition of relatively good language function, 0.2 gram of sodium Amytal was slowly (over a 10 minute interval) administered intravenously. Comprehension of the spoken word as well as the reading ability deteriorated remarkably. All words were enunciated poorly and strange irrelevant words were read into the text.

On September 16, 1947 the patient was talking to his wife who told him that she was preparing to enter the hospital for a thyroidectomy. He had a right sided seizure rather suddenly and was returned to the hospital immediately. On admission he was conscious and was able to express himself appropriately. On being put to bed, he became unaware of his environment and could make no communication. Immediately after unconsciousness occurred, the patient developed repeated convulsions, consisting of clonic movements of the right limbs. These were intermittent and persisted for about one hour. After movements of the right side ceased, the left side began to display clonic convulsions. These persisted intermittently throughout the night. On September 18 when the patient was reexamined, he was completely unconscious. Respirations were approximately 60 per minute. The right upper limb moved about as if he were trying to "wipe sweat from his brow." The right lower limb was flexed at the knee joint. Both left extremities were held in a position of extension but were flaccid. The patient's course continued steadily worse, and he expired without regaining consciousness at 2:20 a.m. on September 19, 1947.

At autopsy, the brain showed generalized arteriosclerosis and atheromatosis. The major cortical lesion was an infarct involving area 22 (caudal part), and adjacent portions of area, 39, 40, 41 and 42 (Brodmann) of the left hemisphere. Subcortically, the lesion extended medially 4.5 centimeters into the white matter. The auditory projection areas appeared to be involved in the destructive process, as was a small area in the posterior thalamus. Two additional small infarcts were recognized in the left thalamofrontal projection system, a third in the pons. An infarct 7 millimeters in diameter was observed in the left neocerebellum. All lesions were old.

Case 3.—A white man aged 50 years was admitted to U.S. Naval Hospital, Bethesda, Maryland, on November 15, 1946. According to the history the patient had been "nervous" for several years. His wife stated that the patient had been drinking heavily for the previous 10 years, and had complained of dizzy spells and swelling of the ankles and legs for the previous five months. He had been admitted to another

hospital on November 13, 1946 for medical observation to investigate the cause of the above complaints. Early on November 15, 1946, while in this hospital, he was found lying on the floor beside his bed, apparently paralyzed on the right side. He was said to be responsive to auditory stimuli. His blood pressure was 150/90 mm. Hg. (left arm). Neurologic examination revealed spastic paralysis and hyperactive deep tendon reflexes on the right side. The Babinski signs were bilaterally positive. A spinal tap was clear; its initial pressure was 120 mm. of water.

Neurologic examination on November 16, 1946 showed a flaccid right hemiplegia with increased deep tendon reflexes and the pathologic reflexes of Babinski and Hoffmann. Hemianesthesia to all the modalities tested was observed. The right side was hyperhidrotic. Gross visual field testing elicited a questionable homonymous hemianopsia (right). The patient had only the ability to repeat the word "no." It was difficult to evaluate his recognition of environmental objects but he was able to eat an orange when presented to him and was able to smoke a cigarette. When asked to raise the paralyzed hand, he often raised the left limb or did not respond to the request. It was evident that he was transiently cognizant of body parts. Singing and humming were apparently not appreciated.

On November 22 he was able to recognize his name when printed for him. He even was able to recognize and carry out simple written requests. About this time certain exclamatory swear words were produced. He apparently recognized their significance. By December 9, 1946 the general picture remained relatively fixed, but when asked to point to parts of his anatomy he often responded with wrong parts. Mimicry was flawlessly executed with the intact limbs.

A further neurologic evaluation on March 22, 1947 disclosed that the right side of the face was statically flat. Dynamic, emotionally triggered face movements were symmetrical. All the cranial nerves were within normal limits of function, except that again a right homonymous "inattention" in the visual fields was seen. Careful tangent screen and perimetric testing showed only a unilateral accentuation of the nasal "hump" of the right eye.

The right upper limb was completely incapable of active movement. This limb was somewhat edematous; because of this, muscle volume change was difficult to evaluate. The limb muscles were under increased tension. The deep tendon reflexes were hyperactive. Hoffmann's sign was strongly positive. Sensory perception to all modalities tested was reduced over the right face and absent over the right upper limb. He was able to walk, using the right lower limb as a static member, mobile only at the hip. The right lower limb was swollen. Deep tendon reflexes were hyperactive. The Babinski sign was positive on the right. Sensation was not appreciated below the patellar region in the right limb. Movements at all joints were symmetrically reduced in force.

Verbalization ability remained approximately fixed. The patient was able to say, "God damn," but this output was less clearly enunciated than on earlier visits. He was able to read short printed words such as "man." His spontaneous writing was limited to a distorted "a." He copied a circle with difficulty. He read numerals and pointed out color charts appropriately. Color matching was not accomplished. His right-left orientation was appropriate. Calculation ability was almost nil. He was able to use comb with his left hand. Because of the sensory deficit of the upper right limb, tactile gnosia was not tested. He was able to carry the tune of "Yankee Doodle." He carried out most verbal requests in an intelligent way. When singing, "America," he occasionally sounded the words "liberty" and "country."

Sodium Pentothal administered intravenously (0.3 grams) failed to alter the verbalization ability significantly. Only very transiently did his "no's" become reduced in volume.

DISCUSSION

Our observations clearly reveal that individuals with relatively focal lesions of the brain show generalized decreased facility in their language function as a primary consequence of a deficit in major speech zones. General cortical anaesthetics, specifically sodium Amytal and sodium Pentothal, fail to differentially inhibit or facilitate any of the prime speech elements for more efficient language function. These findings seem to obviate the presence of a mechanism of psychological suppression or repression as a factor in the blocked volitional verbalization in either the expressive or receptive spheres for the cases here presented. In the terminology of Head,[8] the individuals with irreversible changes in the brain cells appear to have reintegrated their purposive adaptive function into a state of maximum "vigilance." Thus in the case of the vascular lesions there is no reserve; on the contrary, in psychotic cases the apparatus subserving the function of communication is observed to be relatively intact, with ample reserve, when the overall cortical function stabilizes on the different level of action established by the barbiturate drugs.

Certain restrictive limitations to pharmacologic study of language disorders are immediately apparent. Although it has been surmised that the effector element must always precede the braking mechanism (hence the suppressor areas must be more recently acquired than the effector areas), this basic ontogenetic postulate may not necessarily be valid. The differential sensitivity to general cortical depressants of the suppressor and effector areas are not precisely delineated on an experimental basis. Moreover, the injured cortical neurons of the speech areas may be more susceptible to the action of barbiturates than the relatively intact cells comprising the suppressor elements. This would then allow general deterioration of the speech function regardless of the applicability of the law of Hughlings Jackson. Since the lesions in all of our cases, here reported, are the results of vascular insults it must be admitted further than the effect of sodium Amytal is not known on cortical cells which were damaged in the original vascular accident but which subsequently returned to apparently complete normal activity. Moreover, in vascular accidents, particularly those on the basis of arterial hypertension, single lesions must be a rarity.

The use of intravenous sodium Amytal as a means of modifying behavior was first reported by Lorenz[9] and Bleckwenn[10] in 1930. The phe-

nomenon of restitution of communication function was also observed as part of a general return towards temporary normal function in catatonic patients who presented the primary feature of mutism. Solomon[11] and his associates, working with carbon dioxide and with sodium Amytal, presumed a cortical action of these agents because of the effects noted in relieving bulbocapnine action. They further suggested that beneficial effects of sodium Amytal were due to a "bounce-back" following excessive depression of malfunctioning nerve cells. This last assumption was somewhat shaken by Lindemann,[12, 13] who showed that the releasing effect of sodium Amytal could be obtained with dosages less than that producing complete depression of cortical function. Lindemann felt that the drug did not have any specific effect, such as influencing the activities of diseased cortical cells, but that it removed certain inhibitions, which had prevented the individual from manifesting a type of activity more in conformity with his primitive tendencies. Specifically, Lindemann noted that (as compared with alcohol, cocaine, ether) there was a release in inhibition for words, rather than for action, by sodium Amytal. The neurophysiological changes observed suggested progressive depression of cortical function, and further suggested, as did the loss of inhibition, that the most recently acquired cortical functions were first effected by the drug. Subsequent work on sodium Amytal and allied barbital derivatives indicated that it was a general depressant of cortical activity, proceeding from the most recently acquired functions of the cortex to eventual depression of the vital functions in the brain stem.

The simulation, in all respects, of "organic" speech defects by "functional" speech disorders based on anxiety is well known. The interfering effect of anxiety and other emotional disturbances on relearning and retraining processes in aphasia is also commonly accepted. Practical application of this knowledge is found in group retraining activities for aphasics. Participation in group activities with other aphasics removes the element of anxiety and apprehension introduced by competition and/or association with those having full powers of speech. The physiologic substrate of this type of inhibition is not at all clear.

Anxiety and depression arising from interpersonal relations may retard, or may even regress, the course of recovery of a speech defect resulting from irreversible damage to the brain cells. On occasion, psychotherapy aimed towards correction of these influences may greatly enhance the actual demonstrable speech function in a given case. The use of sodium Amytal for the relief of inhibiting anxiety in such cases was described by Linn and Stine.[14] They reported three cases of aphasia, following head wounds, which were considerably improved after ad-

ministration of intravenous sodium Amytal and demonstration to the patient that speech could be relearned. These authors attached great significance to the patients' awareness of speech ability. Unfortunately the cases presented were not detailed enough to determine the exact language disturbance; nor was the post Amytal description sufficient to delineate the cases clearly. The results in our cases, here reported, as well as in three traumatic cases which are a matter of separate report, strongly suggest that the patients of Linn and Stine were suffering from a disturbance of their language function as a result of a general disintegrative process of the interpersonal (emotional) apparatus associated with brain trauma, and not as a result of irreversible structural changes of the major brain areas used in communication function.

Despite the limitations and uncertainties noted, it appears clear that the blocking, or hesitancy of speech formulation, observed in attempted volitional speech output in patients with structural lesions of the brain has a different level of action than the blocking most unambiguously observed in mute catatonic states, and to a lesser degree in other "functional" speech disorders. This fact seems sufficiently well established to allow the use of intravenous sodium Amytal in the differential diagnosis of "functional" speech disorders from those speech disturbances arising on an "organic" basis.

CONCLUSIONS

1. Following the development of gross structural lesions of the brain which involve areas necessary for coded (symbolic) communications, the functionally reintegrated channels of communication experimentally appear to operate without reserve and at almost maximum capacity.

2. By the use of a general cortical depressant no evidence is obtained to indicate that a differentially acting physiologic suppressor apparatus is responsible for the general disturbance in language function that ordinarily follows relatively focal irreversible lesions of the brain.

3. It is evident that the inhibition of verbalization in reversible clinical catatonia and allied conditions is on a different level of function than is the disturbance of language accompanying focal brain lesions in which total communication is influenced adversely.

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• I am unwilling, in view of these facts, to look upon pain as a distinct sense with afferent tracks peculiar to itself; and when we consider also how sensory impressions made on nerves purely of special sense may rise to the height of being painful, it becomes more and more probable that pain is the central expression of a certain grade of irritation in any centripetal nerve.

There is, indeed, every probability that the sensory nerves are competent to carry inward a variety of impressions, which, owing to the peculiar nature of the excitations they cause in the nerve, are capable of appreciation only by the separate centres devoted to their perception, so that pain, touch, and thermal excitations may need, in the peripheral nerves, no different channels for their passage.

It is as if through a single tube were spoken various languages which could be only understood when, at its farther end, they reached the ear of the hearer native to each form of speech. There is in physical science a good deal in favor of the view I have so briefly urged, and, clinically, something may be said for it.

We now know that motor-excitations may be made to pass over sensory nerves, and vice versa, while in most of the instances of loss of pain without loss of tact the lesion has been plainly central. In the rare cases of peripheral analgesia without anaesthesia, it is quite possible that such modifications may have taken place in the nerves as to have destroyed the power of the nerve tissues to transmit particular forms of excitation.

—S. Weir Mitchell in *Injuries of Nerves and Their Consequences*, published in 1872.

Electroencephalographic Foci in Temporal Lobes

With Consideration of Seizure Manifestations

Charles W. Iobst, M.D. and Francis M. Forster, M.D.

As a clinical concept it has been appreciated for a long time that focal seizures may originate in the temporal lobe. The description of uncinate attacks, the dreamy states observed by Hughlings Jackson and certain adversive seizures all pointed to a temporal lobe origin for some of the manifestations of epilepsy. Electroencephalography served as a confirmation of Jackson's concept of epilepsy, and proved that epilepsy is a sudden, disorderly, excessive electrical discharge. The random spike in the electroencephalogram is a well recognized sign of cortical focal discharge.[1, 2, 3] The importance of the spike phase has been emphasized by Gibbs,[4] for a negative spike originating over the cortex indicates a focal discharge at that region.

The role of electroencephalography in temporal lobe epilepsy could well have been expected. To achieve the development of this role, however, it was necessary that the ear electrodes be considerd not ground electrodes but active cortical electrodes sampling the electrical activity of the basal surface of the temporal lobes.[5]

While focal dysrhythmias present themselves spontaneously in some patients with focal seizures, certain methods must be employed to demonstrate the focal dysrhythmia in others. At the present time there are two chief electroencephalographic techniques applicable to temporal lobe lesions. Gibbs and his colleagues[6, 7] demonstrated the value of recording the electroencephalogram during sleep as a means of bringing out focal dysrhythmias. Likewise parental administration of Metrazol serves to indicate the presence of temporal lobe foci.[8, 9]

Employing the various techniques, we have gathered a series of patients with temporal lobe foci associated with seizures. This report is a survey of these patients.

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CASE MATERIAL

Fifty consecutive patients with temporal lobe electroencephalographic foci were studied. In order to gather these cases 2,768 tracings were reviewed over a 26 month period. Among the 2,768 tracings, 255 records were characterized by focal paroxysmal dysrhythmic activity.

All electroencephalograms were made using a standard eight lead placement of electrodes in the frontal, central, occipital and anterior temporal positions over each hemisphere. Electrodes were also placed on each ear. Tracings were made on all patients in the waking state, using an eight channel Grass machine with solder disc electrodes. In those patients studied while asleep the sedation consisted of oral Seconal in dosages varying from 0.1 to 0.4 gm. In four of the early sleep tracings intravenous pentothal was used. During the pre-sleep and during the various phases of sleep the tracings outlined above were made. When Metrazol activation was employed, the intravenous route was used, and 40 mg. of Metrazol were administered per minute.

RESULTS

Paroxysmal electrical disturbances originating in the temporal lobes were picked up by the anterior temporal and/or the ear electrodes. Figure 1 presents the frequency at which each or both of these electrodes served to pick up the paroxysmal disturbance. Approximately one half of the patients' records from both the anterior temporal and the ear electrodes showed the spiking discharges. The anterior temporal leads alone picked up paroxysmal disturbances in 18 cases. The anterior temporal areas, therefore, alone or in combination with the ear electrode, are more commonly the site of origin of epileptic discharges.

Temporal lobe spiking discharges were elicited in the routine records of 26 patients, by inducing sleep in 31 patients and by Metrazol activation in seven patients. Some patients presented the abnormal discharges in more than one type of tracing, and no focus was determined on the basis of single record. Although 26 patients presented in routine records spiking discharges from their temporal lobes, the discharges in only 16 of these patients were sufficiently well established that confirmation was not needed by tracings during other states. In 31 patients, recording during sleep established the presence of a temporal lobe focus. This included 19 patients with normal routine records. In three patients Metrazol activation was necessary to establish the presence of a temporal lobe focus, since both routine and sleep tracings were normal. Therefore, in approximately one half of the patients with temporal lobe spiking discharges

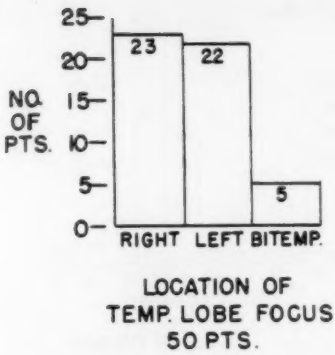

FIG. 1. The laterality and bilaterality of temporal lobe foci determined by electroencephalograph.

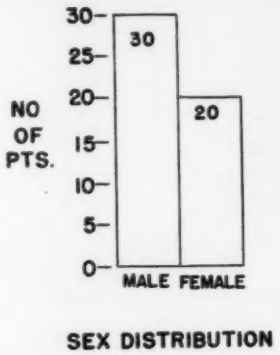

FIG. 2. Sex distribution of patients with focal electrical discharges in temporal lobe.

routine records demonstrate the presence of the focal abnormalities, and in approximately one third of the patients the appearance in routine records is unequivocal. Recording during sleep elicits abnormalities not present in the routine records, and accentuates them when they are equivocal in the routine records. In a small proportion of cases (three in this series) when both sleep and routine records had failed to demonstrate a temporal lobe origin for seizures, the administration of Metrazol demarcated the focal dysrhythamia clearly. In five patients the abnormal firing was bitemporal in origin. The remaining cases were equally divided between the two hemispheres (figure 1). No correlation could be drawn between handedness, laterality of the temporal lobe dysrhythmia and the clinical manifestations of seizures.

This group of 50 patients with temporal lobe foci included 30 males and 20 females (figure 2). The age of onset of seizures is shown in figure 3. The preponderance of males over females, and the high incidence of onset in or after the third decade of life point to a symptomatic origin for the seizures.[10]

The types of seizure (figure 4) present in this group of patients were as follows: psychomotor seizures occurred in 24 patients, grand mal seizures in 31 and jacksonian seizures in 3 patients. Many patients had combinations of seizures. Three patients had no seizures but were studied because of clinical evidence of focal cerebral disease; 11 patients had only grand mal seizures; five had grand mal seizures and abortive auras; 14 had grand mal seizure and psychomotor seizures; nine had psychomotor seizures; one had psychomotor and jacksonian seizures only. Five

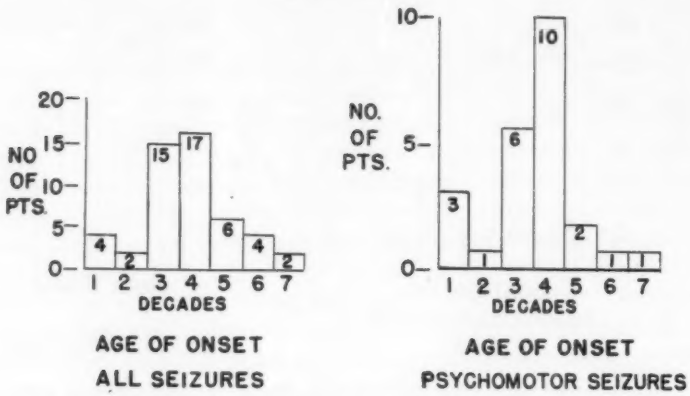

FIG. 3. Age of onset of seizures in patients with electroencephalographic foci in temporal lobe.

patients had atypical seizures.

Psychomotor seizures consisted of periods in which the patient carried out motor or psychic activity which was purposeful but irrelevant for the time and place, and the patient was amnesic for the events of the seizures. Masticatory and uncinate components occurred in many of the patients. Nine of the 11 patients with generalized seizures gave no history, nor had witnesses noted any focal components of the seizures. In these nine patients there occurred no auras which could be construed as indicating an onset of firing from a specific area of cortex, nor was there a focal tonic or clonic onset of the seizure or Todd's paralysis following the ictus.

The five patients with atypical seizures presented a wide range of seizure manifestations. Their attacks were as follows: (a) arrest of motion with maintenance of posture and twitching of the left eyelid; (b) uncinate attacks followed by twitching of right face; (c) vertigo, weakness and motor aphasia for 15 or 20 minutes; (d) uncontrollable rage-like episodes followed by crying but not definitely psychomotor seizures; and (e) temper tantrums with severe occipital headache but without definite disturbance of consciousness.

As noted before, the age of onset of seizures is indicative of a symptomatic origin for the epilepsy. The preponderance of males is also suggestive of this, particularly in the realm of cerebral trauma. On reviewing these 50 cases with temporal lobe discharges, organic cerebral disease was present in 15 patients. Seven patients had undergone severe head injury with skull fracture; only one of these seven patients was seizure free, two

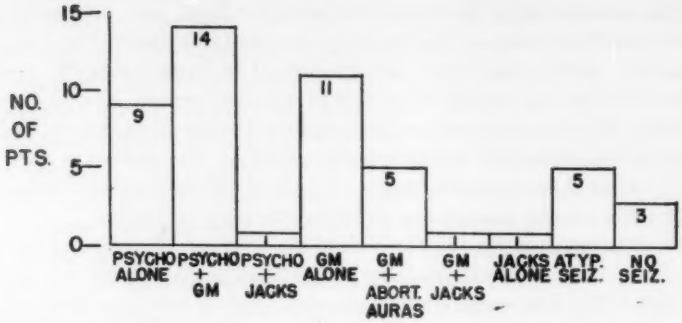

FIG. 4. Types of seizures occurring in series of 50 patients with temporal lobe discharging foci.

had grand mal seizures, one had jacksonian and two had atypical attacks. The entire group included three patients with brain tumors. One patient with a meningioma had no seizures, a patient with an astrocytoma had psychomotor seizures, and another with a glioblastoma multiforme had both generalized and psychomotor seizures. Three patients with unequivocal birth injury all had grand mal seizures and one had, in addition, psychomotor seizures. One patient began to have generalized seizures five years after a course of electroshock therapy and demonstrated a temporal lobe focus. One patient who had had a spontaneous subarachnoid hemorrhage presented a temporal lobe focus but was seizure free. Since this series has been completed we have encountered a patient who had been treated successfully from the serologic standpoint for general paresis but continued to have psychomotor seizures. The definite etiologic factors we have found for temporal lobe focal dysrhythmias then include head injury, brain tumor, electroshock, spontaneous subarachnoid hemorrhage and general paresis.

In this group of patients with cerebral disease as the etiology of their seizure, the location of the temporal lobe dysrhythmia was studied. In six of the 15 patients the anterior temporal lead alone was active, in three the ear electrode only, and in six patients both the ear and temporal lobe lead presented the spiking discharges. No important deduction can be drawn from this.

In these patients with definite evidence of cerebral disease, the temporal lobe foci appeared in routine records in 11 patients, in sleep records in three, and required Metrazol activation in one patient. Incidence of spontaneous focal temporal lobe dysrhythmia is much higher in this group than in the group as a whole.

The presence of an electroencephalographic focus does not necessarily mean that there exists an anatomically demonstrable lesion. The temporal lobes were grossly and histologically normal in three surgically treated patients and in one patient who died of aplastic anemia. The absence of anatomic disorder does not militate against the focus as determined by electroencephalography or electrocorticography, but indicates that the nature of an epileptogenous lesion, or indeed the genesis of epilepsy, is beyond the present boundaries of histopathologic technique.

An attempt was made to correlate the type of clinical seizure with the origin of the dysrhythmia from the anterior temporal, the ear or both electrodes. No firm correlation is possible, but in psychomotor seizures the anterior temporal lead alone was the point of origin in only one of nine cases. This is in sharp contrast to the other types of seizures, particularly in the group with atypical seizures where all five patients had abnormally active anterior temporal leads, and in only one was the ear electrode also active. This series is not sufficiently large to allow deductions from this data.

Twenty-four patients have been followed for a sufficiently long period of time that results of medical therapy can be evaluated and compared with the electroencephalographic changes. The usual and standard anticonvulsants have been employed in the medical therapy, and in addition Phenurone has been administered to those patients not controlled by Dilantin, phenobarbital or similar preparations and in whom there existed no contraindication to an experimental medication. Seven of the 24 treated patients presented their temporal lobe foci in routine tracings. Six of these seven patients were controlled and one was uncontrolled. Fourteen of these patients presented their abnormalities only during sleep records. Seizures were controlled in seven of these, and in the other seven medications were of no avail. Medical control was possible in only one of the three patients whose foci were demonstrated by Metrazol activation. Patients who have convulsive seizures originating in temporal lobe foci are more amenable to medical therapy when the seizures focus is demonstrated by routine electroencephalography than when activation techniques are needed to demonstrate the focus.

The location of the focal dysrhythmia on the temporal lobe could not be correlated with the success or failure of medical therapy. Nine patients had anterior temporal lead foci; five of these were controlled and four were not. Three patients had ear electrode abnormalities only; two were controlled and one was not. Thirteen patients had both ear and temporal electrode abnormalities; eight of these were controlled and five were not. There is no good correlative material in these figures.

Six of the 50 patients in this series have been treated surgically. Two were operated on for the removal of brain tumors. One of these was seizure free prior to operation and has remained so since the removal of a meningioma. The other had an astrocytoma, and while seizure free postoperatively his clinical course is progressively worse. Four patients were operated on for removal of epileptogenic foci. One of these patients, despite negative neurologic examinations, pneumoencephalogram and arteriogram, had a glioblastoma multiforme of the temporal lobe. His grand mal and psychomotor seizures persisted after operation.

Three patients with electroencephalographic evidence of temporal lobe foci were operated upon. Two had lobectomies and one a temporal lobotomy. One of the patients with a lobectomy has not been followed for a sufficient length of time to evaluate; the other lobectomy and the one lobotomy patient have been rendered seizure free.

CONCLUSIONS

This report embodies the observations on a series of 50 consecutive patients presenting temporal lobe focal dysrhythmias by electroencephalography. These focal dysrhythmias appeared spontaneously in 52 per cent of the group. This is a higher incidence than might have been expected. When the dysrhythmia in the routine tracing is not sufficiently clear cut or when, from the clinical viewpoint, a temporal lobe origin is suspected, recording during sleep is mandatory. The clinical factors suggesting a temporal lobe origin are: (a) the presence of psychomotor seizures and (b) the presence of atypical attacks, or major convulsions preceded by factors suggesting on the basis of cortical localization a temporal lobe origin. Using these criteria, recording during sleep established the presence of the temporal lobe focus in 61 per cent of this group. When the clinical situation suggests a temporal lobe origin for the patient's seizures and when both spontaneous records and sleep recordings are normal, Metrazol activation should be employed. By resorting to this we have found an additional three cases of temporal lobe foci in this series. A degree of eclecticism is commendable. Recording during sleep is simpler, less apt to produce a seizure, and sleep is a normal physiologic process. We believe it is, therefore, the preferable method of activation. When a focus is suspected and sleep recording fails, Metrazol activation is necessary, however.

In this series, as in those reported by Gibbs, Gibbs and Fuster[7] the anterior temporal leads most commonly picked up the focal dysrhythmia. The anterior temporal origin is compatible with cerebral damage as the result of relatively mild trauma as pointed out by Gibbs.[7] Trauma, either

birth or postnatal, presumably played a role in 20 per cent of our cases. The age of onset of seizures and the higher incidence of males[10] suggest a symptomatic origin, more specifically traumatic for the origin of the epilepsy. The presence of brain tumor is high in this series (6 per cent).

The emphasis in recent years has been that psychomotor seizures are the epileptic manifestations of temporal lobe lesions. This is not entirely so. Psychomotor seizures most commonly arise from temporal lobe foci. However, other seizure manifestations arise from temporal lobe foci and psychomotor seizures may arise elsewhere. During the gathering of the material recorded in this paper, two cases of psychomotor seizures with frontal lobe foci have been found. In addition there are occasional patients with true psychomotor seizures, occurring in combination with other seizure types and presenting a generalized cerebral dysrhythmia. A note of caution is necessary in concluding that the presence of psychomotor epilepsy indicates temporal lobe abnormality, either structural or electric. In this series only 48 per cent of patients with temporal lobe foci presented psychomotor seizures.

The nature of the electroencephalographic focus offers some suggestion as to the possibilities of medical therapy. This is not the place to enter into a detailed discussion of the medical armamentarium available for the therapy of psychomotor epilepsy. Brain tumor must be considered as a possible genesis of the seizures in each patient with epilepsy and a temporary lobe focus. If a disease process for which surgical therapy is mandatory can be excluded, then the patient with a temporal lobe focus has available both medical therapy and elective surgical intervention. Those patients in this series whose temporal lobe dysrhythmias appeared spontaneously were more amenable to medical therapy than were those patients requiring activation.

SUMMARY

Approximately one half of the patients with temporal lobe seizure discharges in their electroencephalograms have psychomotor epilepsy. Temporal lobe discharges occur in waking records in about one half of cases. Recording during sleep greatly increased the ability to demonstrate temporal lobe foci, but in some cases Metrazol activation was necessary. Etiologic factors producing temporal lobe discharging lesions were head injury, birth injury, brain tumor, electroshock spontaneous subarachnoid hemorrhage and general paresis. Discharging lesions may be present in the absence of gross or microscopic pathologic processes. Medical control of seizures was more easily accomplished when the focal dysrhythmia was elicited in waking records.

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• *Nerves of pain.*—There is a good deal of doubt as to whether or not the various forms of sensory impressions, such as heat, cold, tickling, etc., affect the sensorium through distinct sets of fibres, or whether they travel on a common track with impressions of touch and pain. These latter are, certainly, in a manner distinct; but, although it has been made clear that one or more of the varied forms of sensory expressions may disappear without any other being lost, this is no absolute proof that separate fibres are needed for their conveyance to the centres. Brown-Séquard is disposed to admit the existence of a number of such sets of nerve tubes; but while there is a good deal in general nervous pathology to make it probable that the distinction of sensations depends upon their central discrimination alone, the phenomena of nerve injuries tend to discredit by negative proof the theory of the existence of numerous sets of sensory nerve fibres, as I shall have future occasion to point out.

Of the exact nature of the affection of nerve matter which produces pain we know but little. In general, for the causing of pain we must have mechanical impressions far more severe than those which excite the nerves of tact and temperature; while it would also seem that neural excitation attaining the grade of pain is possible, as in many neuralgias, without the least evidence of visible organic alteration of tissue.

—S. Weir Mitchell in *Injuries of Nerves and Their Consequences,* published in 1872.

Sequelae of Western Equine Encephalitis

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In August and September 1949, 25 patients with western equine encephalitis were admitted to the hospital. The diagnosis was made on the basis of clinical and laboratory studies and later confirmed by an appreciable rise in antibody titer for western equine encephalitis in the patients' sera (table 1). In three of these cases it was possible to establish a specific diagnosis on the basis of the absence of this antibody in the specimens taken during the acute stage of the illness and its appearance during convalescence. Histologic studies on the three patients who died during the acute phase of the illness corroborated the diagnosis. This paper is a report on 15 of these patients whose condition has been followed for six to eight months in an attempt to evaluate possible sequelae.

Previous reports have stressed the infrequency and mildness of residuals.[6-8] Adamson and Dubo,[1] reporting on the Manitoba epidemic of 1941, stated that nearly all of their patients recovered completely. Hammon[2] reported that residuals occur in about 5 per cent of adults and that "most of the reported residuals are in the old age group where it is difficult to assess the damage since arteriosclerotic changes are also present. Tremor, weakness, nervousness, insomnia, mental deficiency and psychosis are the usual end results noted. Parkinsonism is very rarely encountered." Severe residuals have been frequently reported following this illness in infancy.[10-12] Medovy and others[13] have described mental retardation, spasticity and convulsions as common sequelae in children.[3]

The 15 patients included in this study were observed during the acute phase of their illness, and their condition has been followed since then in an attempt to evaluate the sequelae of their infection. This series includes three infants aged 10 weeks and 12 adults aged 17 to 58 years.

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TABLE 1

RESULTS OF NEUTRALIZATION TESTS FOR WESTERN EQUINE ENCEPHALITIS, COLORADO, 1949*

Case	*Age, years*	*Test for western equine encephalitis*	
		Days after onset	*Intracerebral neutralization index*
Infants			
1	10 wk.	18	32
		40	46
2	10 wk.	10	32
		15	100
3	10 wk.	14	100
Adults with maximal residuals			
4	31	6	0
		30	100
		48	187
5	53	7	0
		25	678
6	31	12	187
		24	320
7	53	No serum obtained	
8	58	No serum obtained	
9	54	21	54
		32	320
Adults with moderate residuals			
10	38	15	100
		23	320
		37	187
11	52	5	0
		33	1.000
		53	320
12	55	10	678
		33	320
Adults with minimal residuals			
13	20	16	100
		22	320
		34	320
14	25	8	100
15	17	14	320
		31	678
		45	187

*Virus studies were done by the Communicable Disease Control Center, United States Public Health Service, Virus Research Laboratory, Montgomery 7, Alabama.

The symptoms and the degree of recovery from the infection varied considerably in the two groups. Acute symptoms of the illness subsided sufficiently within two to six weeks after onset to allow discharge from the hospital and convalescence at home. Soon after release from the hospital, the patients returned for psychologic testing and for one or more neurologic examinations. The following psychologic technics were used: (1) Rorschach test, (2) human drawings test, (3) Wechsler-Bellevue intel-

ligence scale for adults, form I, (4) Bender-Gestalt test and (5) Weigl color-form sorting test. Six months after the epidemic, the patients were again contacted. At this time each patient was interviewed by a psychiatrist, examined neurologically, and the same battery of psychologic tests was repeated with the exception of substituting form II of the Wechsler-Bellevue test for form I. Finally, and most informatively, the relative with whom the patient was living was interviewed exhaustively. During this interview an attempt was made to evaluate the patient's pre-encephalitic adjustment and his or her subsequent adjustment. It was observed repeatedly that in response to casual questioning, the patient and frequently the family doctor assured us that recovery was complete, while an interview with interested relatives revealed serious difficulties. In a few cases it was thought desirable to contact social agencies for further investigation of the patient's adjustment.

In the three infants described in this series, the illness began with fever and focal convulsions. These symptoms were followed within a few hours by vomiting, rigidity, stiff neck, twitching and severe dehydration. The temperature attained 103° to 105° F. within 24 hours and returned to normal in three to five days. As the temperature returned to normal, the infants seemed fully recovered; they began feeding normally and were as alert as prior to the illness. Careful examination at this time, however, revealed a hyperreflexia, more marked on the side initially involved with focal convulsions. Follow-up studies have revealed alert, healthy-appearing infants. The principal defect has been an inability to use one side of the body as well as the other. Examination of these children uniformly reveals hyperreflexia with increase in muscle tone of the involved side. The greatest dysfunction is in fine movements and is most apparent in the hand where movements are clumsy and prehensile in character. One of the children continues to have focal convulsions two to three times a week in spite of adequate anticonvulsant therapy.

The clinical course in the 12 adults was far more variable than that described in the infants. The onset was gradual with malaise, drowsiness, headache, back pain and fever being prominent initial complaints. These symptoms increased in all but one of our patients, and progressed to coma in seven patients. Acute symptoms subsided in two to six weeks; following this the patient was discharged. The clinical course varied in severity from that of one patient who complained only of headache, fever, malaise and back pain for several days to that of patients who remained in a coma for 10 to 22 days. The severity of sequelae seemed directly related to duration of coma. Sequelae observed included findings which were present during the acute illness and others which were first

noted during convalescence. Analysis of these symptoms reveals that those which were present most conspicuously during the acute illness have shown the most improvement and are at present of least clinical significance. Prominent among the early symptoms were disturbances in awareness ranging from mild disorientation to coma. Disturbances in sleep are still a frequent but not a serious complaint. An increase in deep reflexes with pyramidal tract signs was a prominent finding in the acute phase of the illness. Hyperreflexia is still common, although abnormal reflexes are no longer observed. Tremor, an early and characteristic finding, was most prominent about the mouth and in the tongue, although it also was observed in the upper extremities. This finding was originally noted in all of these patients but subsided rapidly during convalescence and is now minimally present in six. Eye symptoms have been transient or minimal. Loss of coordinated movement ranged from mild to severe in nine of the patients on testing immediately following the acute phase of the illness. This has noticeably improved in six of the patients on subsequent examination.

All of the patients when first tested psychologically had feelings of physical inadequacy and body weakness. Six of the patients showed anxiety about sensed loss in personality integration, and three reflected a faulty sense of body integration. Six months after the acute phase, they had fewer of these features relating to an awareness of weakness and disorganization. This suggests that there may be an increase in feelings of adequacy in all of these patients.

The sequelae which became apparent during convalescence have not shown improvement and in many instances have progressed. The occurrence of these symptoms is related to the severity of the acute phase of the disease and not to the age of the patient. Residuals are severe in six of the adult patients, moderate in three and minimal or nonexistent in three.

The six patients with severe sequelae varied in age from 31 to 58 years. All of these patients experienced prolonged coma during their acute illness. The clinical syndrome in these patients is characterized by muscle rigidity, speech difficulty, facial masking, loss of weight and severe organic impairment of psychologic function. Associated with muscle rigidity is a slowness, clumsiness and poverty of movement which is particularly evident in the gait. Speech difficulties are common and include a loss of volume or tonal quality or both. In two cases speech remains unintelligible. A progressive loss of facial movements has been prominent and is particularly disturbing to relativees who frequently remark about the peculiar staring expression which is associated with the loss of automatic

blinking movements, and the loss of normal movements of mimicry and emotion. Progressive losses of weight varying from 10 to 40 pounds are present. Distortion of taste is persistent and annoying to five of the patients.

Impairment of intellectual functioning is present in these six patients. Their thinking is vague, poorly expressed, sometimes confused and frequently unrealistic. Capacity to develop new ideas and ability to interpret life situations are impaired. Four of the patients have a loss in ability to abstract, to shift the direction of their thinking if an idea proves inadequate and to learn from experience. There is no difference between the results of the original test and the results of the retest. This suggests that those individuals whose abstraction ability was impaired by the illness remain impaired in this function. Impoverishment of personality resources, marked irritability of emotional reactions and a lack of sustained drive continue to be characteristic of all these patients. Inefficiency in foresight and in planning ability is also evident in these patients.

The three patients with moderately handicapping neurologic and psychologic sequelae demonstrate similar but milder involvement than does the previous group. They seem more aware of and concerned about their residuals. One of these patients was comatose during the acute phase of her illness.

None of the three patients with negligible residuals was comatose during the acute illness. A 17 year old boy, who continues to have multiple complaints, had made an anxious, immature adjustment prior to his illness.

Certain sequelae were not obvious in specific testing situations but became apparent in the total life situation. The patient was often not aware of or concerned about these symptoms, but the immediate family was distressed to note deterioration in loved ones who had been fairly average in their adjustments prior to the illness. For this reason, spontaneous observations by relatives are included in the case reports of the six patients who are most severely handicapped. The case numbers in the following reports correspond to those in table 1.

REPORT OF CASES

Case 4.—A 31 year old male cook became ill on August 22, 1949. He was admitted to the hospital complaining of headache, drowsiness, muscle pain and malaise with a presumptive diagnosis of poliomyelitis. Examination of the spinal fluid on admission revealed an initial pressure of 170 mm. of water with a cell count of 190 per cubic millimeter, of which 92 per cent were lymphocytes, 5 per cent were large mononuclear cells and 3 per cent were polymorphonuclear cells. Chemical studies of the spinal fluid revealed 83 mg. of sugar and 60 mg. of protein per 100 cc. A culture of the spinal fluid

gave negative results. Neurologic examination on admission disclosed a confused and disoriented patient. There was moderate nuchal rigidity, a sucking reflex was obtained, deep reflexes were bilaterally hyperactive and there were bilaterally abnormal plantar responses. Shortly after admission, the patient became comatose and remained in coma for two weeks, during which period his nutrition was maintained by fluids given intravenously and by gavage. Throughout the period of coma he had a temperature of 102° to 103° F. During his illness he was given Aureomycin and penicillin until September 10, 1949, when his temperature returned to normal. At this time his condition seemed greatly improved and he appeared to be making a good social adjustment. He was dismissed from the hospital to the care of his wife on September 15, 1949. The patient was again contacted four months after his acute illness. At that time it was observed that he had almost complete loss of normal facial movements, and both he and his wife complained about the loss of tonal quality in his voice. A moderate resting tremor was noted in the left forearm associated with some cogwheel rigidity in the left arm. The deep reflexes were hyperactive throughout, but were more prominent in the left extremities. The patient himself had no complaints except for the loss of tonal quality in his voice. His wife related that he could not return to work because of hand tremors. She complained that he no longer cared about his appearance, that he drove through red lights, threw bills in the wastebasket remarking they were "only bills," and frequently threatened to harm his family. He spilled food on his clothing and on the floor, and to his family's dismay, he then picked it up and ate it. He did not wait for food to be served, but would snatch it off the platters with his fingers as his wife neared the table. His sexual activity became uninhibited, and he sought intercourse with neighbor children and prostitutes with no concern for possible consequences. He was committed to a state hospital four months after his acute illness.

Case 5.—A tenant farmer aged 53 years was admitted to the hospital on August 20, 1949, complaining of headache, drowsiness and muscle pains, with a presumptive diagnosis of poliomyelitis. An examination of the spinal fluid on admission revealed a pressure of 150 mm. of water with a cell count of 89 per cubic millimeter, of which 30 per cent were polymorphonuclear cells and 70 per cent were lymphocytes. Chemical examination of the spinal fluid revealed 81 mg. of sugar and 60 mg. of protein. A culture of the spinal fluid gave negative results. Neurologic examination on admission disclosed nuchal rigidity and minimal neurologic right-sided findings. During hospitalization the patient was drowsy and could not be aroused for three days. He remained somewhat confused and disoriented for one week. His temperature during the first five days of hospitalization varied from 102° to 104° F. The patient was dismissed on September 20, 1949. He was reexamined periodically, the last examination being on January 26, 1950. At that time, it was observed that the patient's voice was almost unintelligible because of the loss of volume and tonal quality. The patient himself complained of some excess saliva, and a perioral tremor was observed. The deep reflexes were hyperactive, much more so on the left, but no abnormal plantar responses were noted. The patient had marked difficulty with fine movements, particularly with the left hand. The patient's wife complained that although he was unable to work, he found it necessary to keep busy even if it meant just walking around watching the cows. She related that although formerly he paid very little attention to the children, he was now cruel to them. She stated with some pleasure that whereas he had been a domineering household head, he was now no longer interested in being boss and allowed her to buy the groceries with their welfare check.

Case 6.—A 31 year old farmer was admitted to the hospital on September 11, 1949, having been ill for about a week with headache, fever, malaise and photophobia. An examination of the spinal fluid on admission yielded an initial cell count of 40, of which 10 per cent were polymorphonuclear leukocytes and 90 per cent lymphocytes. The spinal fluid contained 67 mg. of sugar and 95 mg. of protein per 100 cc. A culture of the spinal fluid gave negative results. Neurologic examination shortly after admission to the hospital revealed bilateral cogwheel rigidity with a fine right-sided tremor. The reflexes were hyperactive bilaterally, and it was observed that there was an abnormal plantar response on the right. The patient had marked nuchal rigidity. Shortly after admission he became somnolent, although it was possible to awaken him for brief periods of time. He remained in this condition for approximately two weeks, during which time his temperature varied from 102° to 104° F. The patient was dismissed from the hospital on October 12, 1949, to the care of his wife. A reexamination six months after the onset of his acute illness revealed that he had marked loss of tonal quality in his voice, and his wife related that at one time his voice had been almost unintelligible because of the loss of tonal quality and volume. There was almost a complete loss of emotional facial responses. A resting tremor was present, more prominently on the right. There was a loss of fine movements in the right hand and in the right foot, reflexes continued to be more active on the right, and the plantar response was normal. During the interview the patient cried easily in response to rather minimal emotional stimuli. His wife related that he had had two episodes in which his eyes had turned upward and he could not turn them down for a period of 10 to 15 minutes. She also related that he had spells during which he became combative and was out of contact. Even when he was not in one of these episodes, his temper was prone to flare and he was very suspicious. He was rehospitalized in the neuropsychiatric division of a Veterans Administration facility.

Case 7.—A 53 year old white housewife was admitted to the hospital on August 6, 1949, complaining of severe headache, malaise and muscle pain. Examination of the spinal fluid on admission revealed a pressure of 200 mm. of water; 150 cells were observed, of which 75 per cent were lymphocytes and 25 per cent were polymorphonuclear cells. Chemical examination of the spinal fluid disclosed 70 mg. of protein and 80 mg. of sugar per 100 cc. A culture of the spinal fluid gave negative results. A neurologic examination on admission revealed a comatose white female who did not respond. The deep reflexes were hyperactive throughout but more markedly so on the right. Moderate nuchal rigidity was observed with some tremor about the mouth. She remained in coma for 28 days, during which time she received Aureomycin, penicillin, fluids and nutrients intravenously and by gavage. Her temperature throughout this period varied from 101° to 103.6° F. She was dismissed from the hospital on September 20, 1949. On dismissal the patient was able to walk, but since that time she has shown a progression of her symptoms. On February 10, 1950, it was observed that she had a right hemiplegia with a right Babinski sign. It was also observed that her voice lacked both tonal quality and volume, and there was facial masking. There was almost complete absence of fine movements with cogwheel rigidity noted bilaterally. The patient was no longer able to walk in spite of the fact that she had received considerable physical therapy in an effort at rehabilitation. She is being cared for by a sister who relates that the patient cannot walk, dress or eat unassisted. She has fits of laughter during which she is sometimes incontinent and falls to the floor. The husband's and sister's greatest worry is over the patient's lack of concern. The sister stated, "She's

just too contented, makes no plans, doesn't look forward in time, and just lets things happen."

Case 8.—A 58 year old carpenter was found unconscious in his home by neighbors on September 10, 1949 and was hospitalized as an emergency. The patient was alone and no further information was available. Examination of the spinal fluid on admission revealed a pressure of 220 mm. of water with a cell count of 75, of which 65 per cent were lymphocytes. The spinal fluid contained 40 mg. of protein and 80 mg. of sugar per 100 cc. A culture of the spinal fluid gave negative results. Neurologic examination on admission revealed nuchal rigidity which was moderate, an increase in deep reflexes throughout and bilateral Babinski signs. The patient continued in a semicomatose, irrational, febrile state for three weeks, during which time he maintained a fever that ranged from 101° to 102.5° F. With subsidence of the fever the patient's condition cleared within several days, at which time he was dismissed from the hospital. Shortly after he returned home, his wife noted that his voice changed and became almost inaudible because of a loss of volume and tonal quality. Neurologic examination in February 1950 revealed that the patient had a masklike fascies with a loss of almost all tonal qualities of his voice and considerable loss of volume. He had difficulty performing fine movements in both hands. Cogwheel rigidity was observed in both upper and lower extremities, more marked on the right. The deep reflexes were all hyperactive, but no abnormal reflexes could be elicited. The patient's wife related that he was nervous, that he fatigued easily, that he walked with a slow shuffling gait and that he had difficulty with procedures requiring coordination, such as tying his shoes, lighting matches, eating and buttoning his clothes. He no longer could endure being alone and made his wife remain with him at all times. He was unable to sleep. He was bothered by recurring thoughts that he was going crazy, that he was going to die, and he was appalled by silly poems that kept running through his consciousness, for example, "Jesus, lover of my soul, tie me to a fishing pole, if the pole begins to bend, slide me to the other end." He finally made an abortive suicidal attempt and was admitted to a psychiatric hospital.

Case 9.—A 54 year old white married female was admitted to the hospital on August 10, 1949. The onset of her illness dated back to August 6, 1949, at which time she began to suffer from headache, malaise and muscle pains. On August 9 the patient's temperature became elevated to 102° F., an apparent spasticity and tremor developed in the right arm, and she became unresponsive. On admission, examination of the spinal fluid revealed an initial pressure of 250 mm. of water with a total count of 130 cells which were predominantly lymphocytes. Chemical examination of the spinal fluid gave values of 93 mg. for sugar and 132 mg. for protein. A culture of the spinal fluid gave negative results. Neurologic examination on admission revealed a semicomatose, obese, white female with cogwheel rigidity in the right arm and a resting tremor of the right arm. A grasp reflex was also observed in the right arm. There was a clonic, continuous movement of the jaw at a rate of about 3 per second. The patient's fever continued until August 31. Shortly thereafter, she began to respond to stimuli and to eat by herself. Examination at that time revealed some residual tremor bilaterally and considerable loss of volume in her voice. However, no nuchal or cogwheel rigidity was noted. She was dismissed from the hospital on September 21, 1949. The patient was reexamined in February 1950, at which time it was observed that she had considerable loss of volume in her voice, and her family related that the tonal quality of her voice had changed considerably following her illness. Her reflexes were hyperactive

bilaterally, but no abnormal reflexes were noted. No tremor was observed. She did, however, have remarkably poor coordination and an inability to perform fine movements with her hands. The family reported that she was much more careless about her personal appearance and her housework than she formerly was. She was very untidy and appeared to have a loss of normal concern and was unable to care for her own home. Her husband complained that when she decided to retire, she would begin to undress wherever she happened to be, scattering her clothes as she went through the house.

Those patients included in the second group, that is those with moderately handicapping neurologic and psychologic sequelae, have been able to return to former employment. They are maintaining their work level although they sense inadequacies in themselves.

Those with minimal involvement have returned to work and seem to be performing at their former level of functioning. Their relatives express no concern over them.

COMMENT

Severe progressive sequelae have been observed following an epidemic of western equine encephalitis. The severity of sequelae in this epidemic is related to the presence and duration of coma in the acute illness. Three infants included in this series have minimal residual defects. Nine of the 12 adults have sequelae. Six adults with severe symptoms have a clinical syndrome which is similar to the parkinsonism which followed the epidemic of encephalitis lethargica. Neuronal impairment responsible for these symptoms was demonstrated by neurologic and psychologic examinations of the patients.

The sequelae of western equine encephalitis have been reported as frequently severe in infancy and as minimal in adults.[2] Sequelae observed in adults have been described as secondary to the arteriosclerotic changes of senility.[1] The sequelae in our series are not related to aging. Serious and handicapping residuals were observed in young adults with no evidence of vascular disease. Weil[4] has suggested that the virulence of the virus of western equine encephalitis may vary with epidemics. An increase in the virulence of the virus in this epidemic may account for the severe sequelae observed.

The psychological residuals following this illness are difficult to evaluate. Aring[5] has suggested that emotional symptoms following an epidemic of encephalitis may be manifestations of a previous personality disorder. Longitudinal personality studies on all of the patients in this series revealed previous significant maladjustment of personality in only one patient. We feel that there are two other factors which make analysis of these symptoms difficult. The patients with severe psychologic de-

fects are often not aware of their impairment, and families are occasionally pleased with the change in the patient's personality. Follow-up analyses, dependent on questionnaire technics, have been reported[3, 8] and are of dubious value in these cases. The most reliable index of psychologic impairment resulting from this epidemic has been a careful appraisal of the patient's adjustment before and after the acute phase of his illness.

SUMMARY

The condition of 15 patients with western equine encephalitis has been followed for a period of six to eight months. All three infants in the series have an inability to use one side of the body as well as the other, and one has focal convulsions. The severity of sequelae in the 12 adults seem to be directly related to the duration of coma experienced. The sequelae are manifested by rigidity, speech difficulty, facial masking, loss of weight and organic impairment of psychologic functioning. Sequelae have been minimal or nonexistent in three of the adults, moderate in three and severe in six. Three of the patients with severe symptoms have been rehospitalized.

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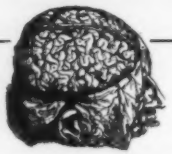

Treatment of Headache

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Discussion of the treatment of headache is difficult because headache is a symptom which may occur in almost any organic or psychogenic disturbance. Therefore, the present paper will be limited to a consideration of some general principles.

Concerning the treatment of headache, the physician has four main methods from which to choose: pharmacotherapy, psychotherapy, physiotherapy and surgery. Each may be tried individually or in combination. The therapist may attempt either to give the patient symptomatic relief or to prevent the occurrence of headache entirely. The latter is obviously preferable, but most of our present treatment falls short of this ideal.

PHARMACOTHERAPY

In pharmacologic treatment we attempt one or more of the following: (1) to raise the pain threshold, (2) to interrupt the mechanism producing pain or (3) to reduce the emotional tension and anxiety associated with the pain.

The efficiency of any drug does not depend on its pharmacological action alone. The importance of dosage, timing and mode of administration cannot be stressed sufficiently. To some extent, also, the effectiveness of the medication depends on the physician who is prescribing the medication, and the length and frequency of his interviews with the patient. It has been observed in many cases that patients maintain improvement if they are seen at weekly intervals but have a recurrence of headache if seen at monthly intervals. The amount of medication must be sufficient and it must be given early in the course of the headache. Treatment of headache may be compared to that of diabetes. If one needs 100 units of insulin and only receives 80 units, the results are therapeutically inadequate. This is especially important with migraine where the ergot derivatives must be given before the vessels have become indurated, and enough must be given to cause adequate vasoconstriction.

In our own clinic we have had the

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opportunity to test a large series of drugs, and have come to depend largely on about a half dozen. Although few in number they are a reasonably adequate armamentarium individually or in combination.

Of those drugs which raise the threshold of pain—the analgesics—only two groups are significant here: (1) the antipyretic analgesics, acetophenetidin and acetylsalicylic acid; and (2) the opium series, including codeine. The use of morphine is contraindicated for treatment of chronic headache for obvious reasons, as are also such synthetic compounds as Demerol and Methadon. While useful agents in controlling pain, the addiction potential and development of tolerance to these synthetic drugs preclude their use in patients with headaches.

The mechanism of antipyretic analgesia is not well understood. It occurs without dulling of consciousness, and there is no marked reinforcement of the action of ordinary narcotics. It has been suggested that these antipyretics relieve pain by affecting not the cerebral cortex but the synapse at some lower level of nervous function, such as the thalamus or spinal cord.[1] An analgesic action may be secured by relatively small doses, such as 10 grains of acetylsalicylic acid or acetophenetidin. Larger doses fail to further raise the pain threshold. Furthermore, if acetylsalicylic acid is used in conjunction with acetophenetidin or codeine, an additive effect is not secured. The pain threshold is raised only to the maximal level of that drug having the greatest effect.[2]

Codeine is the most effective of the analgesic drugs and in small doses (60 mg.) will raise the pain threshold higher than the antipyretic analgesics. In large doses restlessness may be produced. Codeine possesses about a fifth of the analgesic potency of morphine, and causes much less euphoria. It should be noted, however, that codeine and acetyphenetidin are both euphoristic, producing as a central effect a lessening of emotional tension and a sensation of well-being in the patient. Obviously this is a very desirable state for a headache patient and adds to the effectiveness of the medication.

The most satisfactory way to treat headache pharmacologically is to interrupt the pain-producing mechanism. Since many vascular headaches are due to the dilatation and distention of the relaxed cranial arteries, their constriction is the most effective method of treatment. Ergotamine tartrate, an alkaloid of ergot, (Fermergin, Gynergen) produces vasoconstriction of the cranial arteries, reducing the amplitude of their pulsation.[3] This accounts for its effectiveness in the treatment of migraine headaches.

Caffeine, too, is an effective drug in the treatment of migraine. It is often used in conjunction with ergotamine tartrate, and probably acts in a similar way as a vasoconstrictor.[1] There is some evidence that caffeine taken orally may increase the absorption of ergotamine by changing the pH of gastric juice. It also stimulates the central nervous system, reducing fatigue. Caffeine has long been used in the treatment of headache, although its effectiveness obviously will vary considerably with dosage and type of headache under consideration. Doses of 0.1 to 0.5 Gm. have been used successfully.

Certain drugs may be helpful alone or in combination with analgesic drugs by reducing the anxiety of the patient and by changing his mood. The barbiturates are particularly useful as

TABLE 1

MEDICATIONS USED FOR TREATMENT OF HEADACHE

Medication	*Form*	*Amount*	*Action*	*Side Effects*	*Contraindications*
1. Amytal	Tablet	50 mg. (¾ grain)	Sedation		
2. Acetysalicylic acid (aspirin)	Tablet	0.3 gram (5 grain)	Raises pain threshold		Hypersensivity, i.e. nasal congestion with edema, uticaria, asthmatic attacks, etc.
3. Caffeine citrate	Capsule	100 mg.	Vasoconstriction		
4. Codeine phosphate	Tablet	60 mg.	Raises pain threshold	Prostration in cases with severe nausea and vomiting	
5. Dexedrine sulfate	Tablet	10 mg.	Vasoconstriction		
6. Dihydroergotamine methanesulfonate (D.H.E.-45, Sandoz)	Ampule	1 mg.	Vasoconstriction	See ergotamine tartrate—less severe, not as frequent	See ergotamine tartrate
7. Ephedrine and amytal (Lilly)	Capsule	Ephedrine, (0.024 gram, ⅜ grain) Amytal, (0.05 gram, ¾ grain)	Vasoconstriction, sedation		
8. Ergotamine tartrate (Gynergen, Sandoz)	Tablet	1 mg.	Vasoconstriction	Nausea, vomiting, numbness and tingling of hands and feet, muscle pains in thighs and neck, abdominal pain. prostration	Septic infectious states, vascular diseases, coronary sclerosis, history of angina, pregnancy, hypertension, impaired renal or hepatic function
Ergotamine tartrate and caffeine (Cafergone, Sandoz)	Tablet	1 mg. 100 mg.	Vasoconstriction		

TABLE 1—*Continued*

Medication	*Form*	*Amount*	*Action*	*Side Effects*	*Contraindications*
9. Ergotamine tartrate	Ampule	0.5 mg.	Vasoconstriction	Nausea, vomiting, numbness and tingling of hands and feet, muscle pains in thighs and neck, abdominal pain, prostration	Septic infectious states, vascular diseases, coronary sclerosis, history of angina, pregnancy, hypertension, impaired renal or hepatic function
10. Ergotamine tartrate, bellafoline and caffeine	Suppository	Ergotamine, 2 mg. Bellafoline, substance, 0.25 mg. Caffeine, 100 mg.	Vasoconstriction Bellafoline reduces nausea	Nausea, vomiting, numbness and tingling of hands and feet, muscle pains in thighs and neck, abdominal pain, prostration	Septic infectious states, vascular diseases, coronary sclerosis, history of angina, pregnancy, hypertension
11. Glucose	Liquid	50% solution	Reduces brain edema		Dehydration of patient
12. Histamine diphosphate	Ampule	0.275 mg. per cc.	Vasodilatation	Flushing, abdominal pain	Gastric ulcer, cardiovascular disease
13. Neo-synephrine hydrochloride (Stearns)	Liquid	0.5% solution	Shrinkage of nasal mucosa		
14. Nicotinic acid	Tablet	50 mg.	Vasodilatation	Severe flushing, itching, tingling of face and extremities	Sensitivity to drug
15. Phenobarbital	Tablet	30 mg. (½ grain)	Sedation		
16. Privine hydrochloride (Ciba)	Liquid	0.1% solution	Shrinkage of nasal mucosa		
17. Procaine hydrochloride	Ampule	1% solution	Anesthesia		
18. Seconal sodium (Lilly)	Capsule	0.1 gram (1½ grain)	Sedation		
19. Sucrose	Liquid	50% solution	Reduces brain edema		Dehydration of patient

synergists by adding their sedative effect. Chemically related to urea and to hypnotics of the carbamate series, barbiturates have an effect on the central nervous system that is essentially sedative and hypnotic. They must be used judiciously, however, because of the danger of addiction. In general an intermediate (Amytal) or shortacting (Seconal) barbiturate is the most satisfactory in headache cases. Amytal is usually given in doses of ¾ grain, (50 mg.), Seconal in doses of 1½ grain (0.1 Gm.).

The accompanying table outlines some of the medications used for the treatment of headache, together with dosage and action of each.[4]

Some of the more common reasons for failure in therapy are as follows: incorrect diagnosis; inappropriate, inadequate, or improper administration of medication; inflexibility of therapeutic regime; failure to recognize the variable etiology of the syndrome; additional factors associated with the attack; and finally the vital role of the patient-physician relationship.[5]

PSYCHOTHERAPY

Whenever psychotherapy is indicated, the first problem is adjustment to psychological treatment itself. There are still millions who need to accept such treatment, and yet believe that a visit with a psychiatrist is reserved for "crazy people." There are other millions with the firm belief that treating a real pain by "just talking" is the most arrant nonsense. To get such patients to accept psychotherapy is always difficult and sometimes impossible.

A fact which should be well known, but is too often lost sight of, is that the most important single factor is the emotional relationship between the patient and the physician. In psychoanalytic treatment, of course, this relationship becomes a fundamental subject of discussion. In other less intensive and more common forms of therapy the relationship still dominates the treatment although it may be explicitly discussed only rarely or not at all. Therefore, it is vital to the therapist to feel this relationship keenly at all times in order to understand, forecast and skillfully direct the course of treatment. Facts otherwise unintelligible become readily understandable in the light of this awareness.

In emphasizing the importance of the physician-patient relationship we must not overlook other aspects of psychotherapeutic procedure, such as environmental manipulation and the ventilation of wholly or partly unconscious emotional conflicts.

In environmental management one has to recognize and deal with the patient's capacity to handle his work, recreation, family and social life. The physician should strive to correct the patient's program so that work, play and rest are balanced. In some cases a sustained hobby is of value in securing relief from tension and daily stress. Concerning any changes in the patient's way of life, it is important that the doctor assist the patient in making his own decisions rather than that the physician make such decisions himself.

Often it is more practical and more satisfactory to have the patient adjust to his environment rather than alter the environment. This is done by "ventilation"—having the patient talk out his problems with the aim of gaining greater understanding of his emotional life and difficulties. He may thus achieve freedom from needless anxiety, enabling him in turn to cope with actual stress situations. The physician must learn to listen patient-

ly and create an atmosphere of trust and confidence.

Sometimes explanation of the effect emotions have on bodily functions and the relationship of stress situations to one's own symptoms may demonstrate simple psychosomatic theory and give the patient insight into what occurs during periods of strain.

Reassurance, suggestion and re-education are other technics which may help the patient gain the necessary security and readjustment to life.

The physician may find in some cases that the contribution of a psychologist or social worker will aid in an understanding of a patient's personality. Furthermore, a social worker can help in technical advice and in finding community resources for the individual and family.

PHYSIOTHERAPY

The use of physiotherapy in the treatment of headache is limited. When extracranial structures of the head and neck are involved, massage of neck muscles and support of the head by a cervical collar, bandage or traction by head halter may be of value. Injection of procaine hydrochloride 1 to 2 per cent into tender areas is a helpful adjunct to this type of therapy. The use of histamine or metacholine by iontophoresis may help promote increased circulation and relaxation. Warm baths of 30 minutes duration twice daily are useful, in migraine as a prophylactic measure, in tension headaches to secure symptomatic relief.

SURGERY

The treatment of headache by surgical technics is limited largely to a few specific conditions wherein the operation can be directed toward a primary agent; however, it occasionally can be aimed toward interrupting the aggravating nerve supply. There are many reports in the literature of operative procedures for various types of headache.[6, 7, 8] In evaluating these, it must be remembered that headaches are often improved or eliminated during hospital stay or prolonged convalescence alone, probably by coincidental reduction of stress and responsibilities. The following are some of the conditions in which head pain has been lessened by surgery.

In the presence of an intracranial mass such as glioma, meningioma, abscess, subdural hematoma, aneurysm or other mechanical lesion neurosurgery is required. Headache associated with glaucoma may necessitate surgical decompression of the eyeball to save vision, an operation which has a secondary salutary effect of reducing the intensity of the headache. Headaches developing from cervical disc, cervical rib and the scalenus anticus syndrome may be relieved by surgical approach to these offending areas.

Growths in the area of face, head or neck often require surgical intervention for the relief of intractable pain. Section of cranial nerves supplying these areas will usually eliminate this pain. However, in the case of the ear, rather extensive section of the cranial nerves is required, and may include the seventh and ninth and roots of the tenth cranial and upper cervical nerves to eliminate the pain. In most cases, subtotal section of the fifth cranial root eliminates the pain in a wide area of the face. If the pain is in the base of the tongue, tonsils or throat the ninth cranial nerve is sectioned.

In trigeminal neuralgia (tic douloureux) it is usually necessary eventually to section the sensory root of the fifth. Trigeminal neuralgias resulting from tumors involving the

sensory root or ganglia are obviously surgical situations. Glossopharyngeal neuralgia is treated by resection of the offending division.

Headaches are often an accompaniment of hypertension. The use of the Smithwick sympathectomy in certain expertly selected cases has been suggested as a means of lowering blood pressure and eliminating headache. Despite the fact that the direct correlation between height of blood pressure and severity of headaches has never been shown clearly, the operation often accomplishes symptomatic relief. One might bear in mind that the nonspecific effects of hospitalization and lessening of stress may in themselves reduce the headache in these cases by slightly lowering the blood pressure.

Surgical treatment of migraine has been recommended by many investigators.[6] Operative methods include arterial ligation, section of the supraorbital, occipital and middle meningeal arteries and external carotid artery. The results have been unsatisfactory and improvement only temporary in most cases. Other surgical procedures suggested are fractional section of the posterior root of the trigeminal nerve and parasympathectomy. The inconsistency of results makes this approach somewhat impractical.

Lobotomy, thalamotomy, lobectomy and topectomy have all been recommended for the relief of intractable pain and for exaggerated pain response in the presence of long-standing emotional instability.[8] The present data on such radical therapy indicates that the effect of psychosurgery on pain is rather unpredictable. Further studies are necessary before a critical appraisal of these techniques can be made.

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Neurology

Clinical Pathologic Conference

From the Department of Neurology and the
Laboratory of Neuropathology, Philadelphia General Hospital

Presented by Charles Rupp, M.D. and Helena E. Riggs, M.D.

PRESENTATION OF CASE

A 65 year old male negro was admitted to the neurologic service of the Philadelphia General Hospital on May 22, 1950, because of inability to speak and right-sided weakness. It was impossible to obtain an adequate history.

Physical examination revealed a normally developed and well nourished elderly colored man who was somnolent but could be easily aroused. The heart was enlarged to the left, and there was an apical systolic murmur. Blood pressure was 146/80. There were a few fine rales in the left lower base. The vital signs were within normal limits otherwise, and the remainder of the general physical examination revealed no pertinent abnormalities.

Neurologic examination revealed mixed expressive and receptive aphasia, anomia and possibly apraxia. The pupils were equal, regular, reactive to light and accommodation. Examination of the optic fundi revealed moderate angiosclerosis, but otherwise there were no abnormalities. There was a slight right hemiparesis. All of the deep tendon reflexes were depressed. No pathologic reflexes were elicited. No sensory abnormalities were noted.

Laboratory studies: Urinalysis and a complete blood count were within normal limits; the blood serology was positive with 4 Kahn units; blood sugar was 125 mg. per 100 cc.; the blood urea nitrogen 8 mg. per 100cc.

Spinal puncture revealed an initial pressure of 160 mm. of water. There were no cells. The total protein was 80 mg. per 100 cc.; the spinal fluid serology was negative; the colloidal gold curve was 1122100000.

Roentgenograms of the chest revealed the lungs to be clear, the heart enlarged to the left, and the aorta slightly tortuous. A roentgenogram of the skull was negative; and a roentgenogram of the dorsal and lumbar spine revealed only mild degenerative arthritis.

Clinical Course: The patient remained somewhat lethargic. Two days after admission it was noted that his pulse had fallen to 48 per minute. Treatment was supportive and his condition fluctuated. Two weeks later neurologic reexamination revealed the right pupil to be slightly larger than the left. There was a right hemiparesis with an equivocal right Babinski sign. The blood pressure at this time was 160/110, and the pulse rate was 60. A repeat spinal fluid examination revealed

initial pressure of 200 mm. water, with two leukocytes per cubic millimeter and a total protein of 80 mg. per 100 cc. Thereafter his condition improved. One week later the patient was able to answer a few simple questions, but it was obvious that there was a severe aphasia. Aside from a prolapse of the rectum which was treated conservatively after proctoscopy, the patient continued to do fairly well and had no complaints of headache. He was able to sit up on the ward. Three months after admission he was found in a deep coma. Blood pressure was 180/95, with a pulse rate of 56 and a respiratory rate of 16. Examination of the fundi revealed papilledema of two to three diopters with hemorrhages about the discs. There was a flaccid quadraplegia with absence of all the deep tendon reflexes. The blood pressure fell, the pulse became rapid and thready, and the patient expired two days later.

DISCUSSION

DR. CHARLES RUPP: This patient illustrates a clinical picture frequently encountered on a large neurologic service. An individual in the later age decades with hypertension presents the clinical findings of a focal neurologic lesion. The x-ray of the skull, eye ground examination, spinal fluid and other studies fail to reveal any other cause for the patient's condition. It is assumed that the neurologic signs are due to cerebral vascular disease. Because of age and poor general cardiovascular status, little or no attempts at therapy are made and the patient tends to be relegated to a less conspicuous part of the ward where he is lost in the shuffle of a busy admission service. Suddenly the patient becomes worse, and reexamination reveals indisputable evidence of increased intracranial pressure far beyond what might be anticipated on the basis of cerebral vascular changes. Suspicion is then aroused that the symptoms have, from the onset, been due to an intracranial mass lesion, but it is too late for effective surgical intervention and the patient expires.

Although the blood serology was positive, quantitatively the Kahn showed only 4 units. The spinal fluid and clinical findings did not suggest the presence of central nervous system syphilis, and I do not feel that lues need be seriously considered as an etiologic possibility. Elsewhere, attention has been called to the fact that the presence of a positive serology may be misleading.[1] I have seen many patients whose neurologic symptoms were thought to be luetic in origin because of a positive serology but, at post mortem, they were found to be suffering from a non-luetic neurologic condition.

The diagnosis of a mass lesion might have been suspected earlier if greater attention had been paid to the presence of a slow pulse and the rather prolonged lethargy which is somewhat unusual, but not incompatible with a cerebral vascular condition. When a slow pulse is encountered in individuals with cardiovascular disease, it is frequently attributed to heart block; and one does not think of bradycardia associated with increased intracranial pressure, particularly when the spinal fluid and fundus examinations do not confirm the suspicion of intracranial hypertension. The only abnormalities noted in the cerebrospinal fluid examination were the increased protein and the changes in collodial gold reaction which are not infrequently found in patients with cerebral vascular disease. The possibility of a mass lesion can, at times, be ruled out only by pneumoencephalographic studies, but hypertensive patients with poor general circulatory apparatus do not usually

respond well, and the dangers of subjecting them to encephalography are great.

Ultimately, the patient developed unequivocal evidence of increased intracranial pressure. This, along with the progressive downhill clinical course, justifies a diagnosis of a primary intracranial tumor. While the patient had evidence of cerebral vascular disease, attribution of his symptoms to a vascular cause is fallacious *post hoc propter hoc* reasoning.

Clinical Diagnosis: (1) Hypertensive cardiovascular disease, with cerebral vascular accident. (2) Brain tumor suspect.

Dr. Rupp's diagnoses: (1) Brain tumor primary, left frontotemporal area. (2) Generalized and cerebral arteriosclerosis.

PATHOLOGIC EXAMINATION

DR. HELENA E. RIGGS: *Anatomic Diagnoses:* Cystic glioma, left temporal lobe. Increased intracranial pressure. Terminal hemorrhagic necrosis of tegmentum and tectum of the midbrain.

At post mortem the brain was greatly swollen and congested. The cortical veins were over-filled to the point of thrombosis. The cortical markings were obliterated and the left temporal lobe appeared disproportionately large. The tissue here was soft and cystic to palpation. There was a large well-formed cerebellar pressure cone, and on the left the swollen temporal lobe compressed the cerebral penduncle. The optic tract and the uncus were herniated through the tentorial notch. On section, there was very marked edema of the entire left hemisphere. In the temporal lobe, just below the cortical grey ribbon, the tissue appeared distinctly abnormal although no definite neoplasm could be distinguished. There was, however, a cystic area containing a yellowish viscid fluid. The tissue surrounding this was soft and yellowish with areas of necrosis and hemorrhage. Due to the edema of the left hemisphere, the lateral and third ventricles were distorted. The body of the left lateral ventricle was smaller than the right, and the anterior portion of the third ventricle was compressed. The neoplastic tissue appeared to occupy the subcortical white matter and did not involve the striatum or the internal capsule. There was an area of terminal hemorrhagic necrosis involving the entire tectum and tegmentum of the midbrain. The cerebral vessels showed severe atheroma. Microscopic examination revealed an astroblastic glioma (undifferentiated astrocytoma). The terminal circulatory collapse was most likely due to the rapidly increasing intracranial pressure which resulted in hemorrhage into the midbrain.

DR. RUPP: From the practical therapeutic standpoint, failure to diagnose the presence of a tumor in cases such as this is not as tragic as it might at first appear. These elderly patients with diseased cardiovascular systems are poor surgical risks, and even if the tumor has been recognized and approached surgically, the prognosis would be extremely poor. Rarely the tumor is a meningioma but more often it is a more malignant tumor, either primary or metastatic, and I do not feel that life expectancy was materially shortened by the failure to recognize the true nature of the pathology earlier in the course.

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Neurology

.....BOOK REVIEWS....

The Collected Papers of Adolph Meyer

Eunice E. Winters, General Editor, with an Introduction by Louis Hausman, M.D. 1950. Baltimore: The Johns Hopkins Press, 693 pages, $7.50.

Throughout his long life dedicated to the advancement of neurology and psychiatry, Dr. Adolph Meyer wrote many papers which were published in current medical periodicals, but he wrote no books. Miss Eunice Winters, together with the assistance of Drs. Solomon Katzenelbogen, Louis Hausman, Franklin G. Ebaugh and Alexander H. Leighton and Sir David K. Henderson, has collected 250 of the most significant of these papers, and has divided them into volumes according to subject matter. Volume I dealing with neurology was edited with the assistance of Dr. Hausman and contained nearly eighty papers.

Many of the younger neurologists of today are not aware that Dr. Meyer's original field of endeavor was neurology and that his approach to psychiatric problems developed as a result of his interest in the interrelationship between neurology and psychiatry. The majority of his publications during his formative years dealt with neuroanatomy, neuropathology and clinical neurology. Even after he had assumed the directorship of the Henry Phipps Psychiatric Clinic, he maintained a productive neurologic laboratory and conducted an elective course which dealt with the functional anatomy of the nervous system. His concept of the segmental and suprasegmental levels of the nervous system is the basis for his later theories of psychobiology.

The papers of this volume are divided into three main groups: neuroanatomy, neurology and neuropathology. In the first group are contributions on comparative neuroanatomy, on reconstruction of serial sections of the brain, on the auditory nerves, and on the optic radiations including the temporal lobe detour known by many as Meyer's loop. Under neurology are many papers dealing with Meyer's concepts of aphasia and others concerned with syphilis of the central nervous system, neoplasms and trauma, as well as case reports. Under neuropathology there are many case reports, including two discussions of the subject of "central neuritis."

The articles in this volume are still of current interest. They are reproduced in full, many of them with excellent color illustrations. This book not only serves as an outstanding reference source to fundamental contributions in neurology, but also is an excellent historical treatise on the development of this subject in the last decade of the 19th century and the early part of the 20th century.

R. N. DeJ

NEWSLETTER

JULY-AUGUST, 1951

Pearce Bailey, President
Howard D. Fabing, President-Elect
Walter O. Klingman, Vice-President
Francis M. Forster, Secretary
Joe R. Brown, Treasurer

AMERICAN ACADEMY OF NEUROLOGY

Plans Shaping for Louisville Meeting Plans for the 1952 Academy meeting at Louisville (April 24 and 25) are moving into high gear. Headquarters will be at the Brown Hotel which offers unique facilities. . . . The regular sessions will be preceded by specially designed review courses in neuropathology, neuroroentgenology and electroencephalography. As at Virginia Beach, there will be a half-day joint symposium with the American League Against Epilepsy. . . . Authors are reminded that titles of papers accompanied by 50-word abstracts should be submitted (not later than November 1, 1951) to Dr. Alexander T. Ross, Chairman, Scientific Program, Indiana University Medical Center, Indianapolis, Ind.

Neurology in Louisville Louisville has added another laurel to its fame as a place of distinctive achievements. A neurology department has been developed at the University of Louisville by E. Roseman, professor of neurology and departmental head. The program encompasses the neurologic activities of the Louisville General Hospital and the Nichols Veterans Hospital—both of which have approved residencies in neurology. Active research is pursued in four well equipped laboratories and follows a clinical pattern associated with electroencephalography. Academy members associated with Dr. Roseman are R. P. Schmidt, Lewis Levy and I. O. Dein.

A Message from Auxiliary President Mrs. Frederick P. Moersch, president of the Women's Auxiliary to the AAN, sends a letter of greetings in which she remarks on the attendance of the Auxiliary (over 50 per cent of the membership) at the Virginia Beach meeting, and points to the importance of all auxiliary members becoming actively affiliated with organized medicine, particularly neurology. The Auxiliary president also urges members to plan now to attend the Louisville meeting; to mobilize their special talents to furnish an arts and crafts exhibit or other form of interesting display for this meeting; and to scan regularly the Newsletter in their husband's copy of NEUROLOGY for items of interest to the Auxiliary.

Committee Chairmen Appointed Pursuant to Academy policy all committees became dissolved with the taking of office of the new Academy officers at the Virginia Beach meeting (April 13). At this writing, the following committee chairmen had been appointed: M. T. Moore, auditing; C. G. de Gutierrez-Mahoney, constitution and by-laws; R. N. DeJong, editorial board (NEUROLOGY); A. B. Baker, education; Edwin G.

Zabriskie, ethics; A. B. Baker, federal affairs; Webb Haymaker, history; Benjamin Boshes, International Neurological Congress; D. B. Ruskin, legislative; C. H. Millikan, membership; J. E. Skogland, nominating; H. D. Fabing, program (general); A. T. Ross, program (scientific); Royal C. Gray, survey. . . . Any members desiring to serve on a committee should communicate with the president.

Additional Members from Abroad Six distinguished neurologists from abroad recently were admitted to membership in the Academy. The new honorary corresponding members are: Prof. Dr. Vicente Dimitri, (Argentina); Prof. Van Gehuchten, (Belgium); Prof. G. De Morsier, (Switzerland); Prof. G. Pamboukis, (Greece); Prof. Dr. M. Nonne, (Germany); Prof. M. Kaila, (Finland). Honorary corresponding members previously elected to the Academy are listed in the January 1951 number of the Newsletter.

NANDBC Holds Third Meeting The National Institute of Neurological Diseases and Blindness Council held its third meeting June 4 at the National Institutes of Health, Bethesda, Md., with Dr. David Price, associate director, National Institutes of Health, presiding. It was announced that the appropriation contained in the President's budget for this newly created institute had been passed by the House and was now before the Senate. To date no action on this bill has been reported out of the Senate. Until this Institute has its own appropriation, it lacks operating funds, and at present its affairs are being administered by the National Institute of Mental Health. However, since the National Institute of Mental Health and the National Institute of Neurological Diseases and Blindness are to have a joint scientific director, an appointment to the post has been made. The recipient is Dr. Seymour S. Kety, professor of clinical physiology at the Graduate School of Medicine, University of Pennsylvania. Dr. Kety is particularly known for his work on cerebral circulation and metabolism.

New Training Course in Epilepsy and EEG Announcement has been made of the inauguration of a training course in the diagnosis and treatment of epilepsy and in electroencephalography to be conducted at the Seizure Division of the Children's Medical Center in Boston, under a special grant from the Children's Bureau, acting through the Massachusetts Department of Public Health. A limited number of physicians and prospective EEG technicians will be accepted. The first course begins July 1, 1951. Details may be secured from state or territorial health departments, or from Dr. William G. Lennox, 300 Longwood Avenue, Boston, Mass., who will have general direction and to whom applications should be made.

Digest of Paris Conference Reaches U. S. The third and final volume of the Digest of the Fourth International Neurological Congress (Sept. 5-10, 1949) has arrived in this country. The first two volumes of this digest, which con-

tain abstracts of papers presented at the scientific sessions, were issued at the time of the Congress (See October 1949 Newsletter). This third and final volume contains abstracts of papers not included in the first two volumes; two complete papers: one by Wilder Penfield on the clinical classification of the epilepsies—the other by Andre-Thomas on the works of Dejerine; and in addition, the makeup of the offical committees, a statement of the resolutions passed during executive sessions, as well as a list of the names and addresses of all members of the Congress from all countries. The editor of the Digest is Dr. Raymond Garcin, secretary-general of the Congress. The publishers are Masson et Cie, 120 boulevard, St.-Germain, Paris (Vle).

* * * * * *

Contributions to the AAN At the Virginia Beach meeting a new plan was approved to permit members to make voluntary contributions to the Academy simultaneously with the payment of annual dues. Accordingly, the 1951 statement of dues will contain provisions for members to make individual contributions to the Academy—if they find it convenient and desirable to do so. The purpose of the plan is to provide the Academy with additional funds without increasing annual dues. These supplementary funds are needed to activate certain Academy projects which have been designed to implement neurology and add to our knowledge of the nervous system. . . . More detailed information concerning the plan, together with a list of Academy projects, will be contained in a cover letter accompanying the annual statement of dues. . . . It is hoped that contributions, when made, will be on a free and voluntary basis and represent a form of annual giving for the advancement of medical science.

Epilepsy Institute Meets in Salt Lake City The Third Western Institute on Epilepsy was held at the Hotel Utah, Salt Lake City, June 22-24. The Institute was presented as a memorial to Dr. Jerry Price, whose untimely death last September ended his notable career in neurology and epilepsy. The program comprised papers and demonstrations on epilepsy in its therapeutic, research and socio-economic aspects. Tracy Putnam gave the keynote address on the evaluation and future of the treatment of epilepsy.

American Board Meets in Philadelphia The American Board of Psychiatry and Neurology held its spring examinations June 11-12 in the various facilities of the Philadelphia General Hospital. Approximately 350 candidates presented themselves for examination. A list of the successful candidates in neurology will be published in the next issue of the Newsletter.

Briefs Joe R. Brown reports that Dr. E. Grahame Robertson, distinguished neurologist from Melbourne, Australia, recently gave a series of lectures at the Mayo Clinic. Dr. Robertson

also attended the neurological meetings in Atlantic City (June 16-20), and has departed for a visit to England where he can be reached through Dr. Dennis Brinton, 60, Frognal, Hampstead, London. He expects to complete his tour in the U. S. in September, visiting in New York (Sept. 3-16); Baltimore (Sept. 16-24); and Washington (Sept. 24-28). . . . Morris Bender, professor of clinical neurology, New York University College of Medicine, has accepted an additional appointment as neurologist to the Mount Sinai Hospital as of June 1. . . . Augustus S. Rose is now professor of neurology at U.C.L.A. . . . Henry R. Viets of Boston has accepted appointment as lecturer in neurology and in historical and cultural medicine at the University of Texas Medical Branch, Galveston. . . . Francis J. Braceland, chief of section, Mayo Clinic, and secretary of the American Board of Psychiatry and Neurology, will take office in July as psychiatrist-in-chief to the Institute of Living, Hartford, Conn. . . . The newly elected officers (May 8) of the APA are D. Ewen Cameron, Pres.-Elect; R. Finley Gayle, Jr., Secy.; and Howard W. Potter, Treas. . . . The rapidly expanding neurology service of A. Theodore Steegmann at the University of Kansas Medical Center, has a vacancy. This program is approved by the Council on Education of the AMA. . . .

Percival Bailey

Cerebral Palsy

John F. Pohl, M.D. 1950. St. Paul: Bruce Publishing Company, 224 pages, $5.00.

This book speaks eloquently for the present status of the cerebral palsy problems; namely, an empirically set up series of treatment methods which in this instance are obviously the result of personal observation of the author.

The greatest weakness in this exposition is the author's inadequate knowledge of neuroanatomy and neurophysiology, upon which he depends for his explanation of the physiologic mechanisms he describes in his cerebral palsied patients. The weakness of his neuroanatomy is illustrated by such statements as "The atonic type of cerebral palsy is marked by flaccidity of the muscles and possibly results from a lesion of the premotor area of the brain." Whereas it is known that a very limited part of the precentral motor cortex, or area 4, from which "flaccidity," if it be of cortical origin, can be obtained. In discussing his so-called "spastic type" of cerebral palsy (of which 66 per cent of the whole group is classified) he gives his opinion that most of these originate from cortical lesions, overlooking the fact that considerable cortical tissue would be involved in the cases he describes and that it is more likely that subcortical lesions in motor pathways provide the focal points for the activation of muscle tonus.

Pohl's classification of types of cerebral palsy is quite empirical and confusing since semantics seem involved. His use of terms "spasticity" and "rigidity" is not clear. "Spasticity" is characterized by "stiffness," he says. (The reviewer thinks of "stiffness" in relation to joints and overworked muscles.) "Rigidity" is a state of "plastic hypertonus," and his illustration (Fig. 7) shows a child illustrating decerebrate rigidity, which he says is due to "widespread brain damage." Not once does he allude to choreic movement; indeed seldom is a case of athetosis seen free of choreic movement. Torsion and ballistic movement is not mentioned though these are elements of disorder of the upper brain stem, which is frequently damaged in hypoxic states at birth. Whereas the author finds purity of his forms, neurologists and their books indicate the great admixture of symptoms and combinations of abnormal movement and kinds and disposition of tonus.

On the whole, as far as technical procedures are concerned, the occupational therapy section is better than that devoted to physical therapy.

M. G. M.

The Neurosurgical Treatment of Traumatic Paraplegia

J. Lawrence Pool, M.D., Professor of Neurological Surgery, College of Physicians and Surgeons, Columbia University. 1951. Springfield, Illinois: Charles C. Thomas, Publisher, 107 pages, $3.00.

This brief monograph, one of the American Lecture Series, deals with the classification, pathologic physiology, diagnosis and treatment of spinal and spinal cord injuries. Unfortunately, in view of the title, a large portion

of the book is devoted to classification, pathophysiology and diagnosis, and only a small part of the volume deals with treatment, especially with neurosurgical treatment, of vertebral and cord injuries. The control of mass spasms which, it seems to the reviewer, is one of the major problems in the treatment of traumatic paraplegia, is dealt with in slightly more than two pages, in which as many lines are devoted to the use of sodium Dilantin for alleviation of spasms as to the use of either rhizotomy or dorsal column section.

A very important section of the book, one which contains the most essential data, is the final chapter on "Management of the Paraplegic Patient" in which the author outlines, in some detail, the care of the bladder, management of decubiti, avoidance of respiratory and abdominal complications, morale, and rehabilitation.

R. N. DeJ.

Genetic Neurology

Problems of Development, Growth and Regeneration of the Nervous System and of its Functions

Paul Weiss, Editor. 1950. Chicago: University of Chicago Press, 239 pages, $5.00

Genetic Neurology is a symposium of essays written for the first meeting of the international conference on the development, growth and regeneration of the nervous system which was held at the University of Chicago, March 21-25, 1949, under the sponsorship of the International Union of Biological Sciences. It deals with what is termed a new scientific discipline, "genetic neurology." It is stated by the editor, Dr. Paul Wiess, professor of zoology at the University of Chicago, that neuroanatomy, neurophysiology and neuropsychology deal essentially with the nervous system in its final, mature state. Genetic neurology, on the other hand, encompasses all those processes that lead up to that state, maintain its integrity and restore it after disruption. The papers published in the volume deal with such subjects as the differentiation of central nervous system and of its units; the outgrowth of nerve fibers and establishment of nerve connections; the growth and trophic relations of neurons; the regeneration of nerves, including its implications for the clinical problems of nerve repair; the problems of specificity and selectivity in the development and operation of the nervous system; the development of behavior and its neural foundations. Among the contributors are Drs. Donald H. Barron, professor of physiology at Yale University; David Bodian, associate professor of epidemiology at Johns Hopkins University; Jan Boeke, professor emeritus of histology and embryology at the University of Utrecht; R. W. Gerard, professor of physiology at the University of Chicago; Davenport Hooker, professor of anatomy at the University of Pittsburgh; Holger Hydén, professor of histology at the University of Göteburg; Sydney Sanderland, professor of anatomy at the University of Melbourne; William F. Windle, professor of anatomy at the University of Pennsylvania; and J. Z. Young, professor of anatomy at the University College, London.

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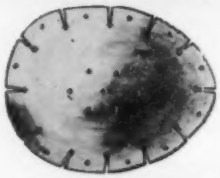

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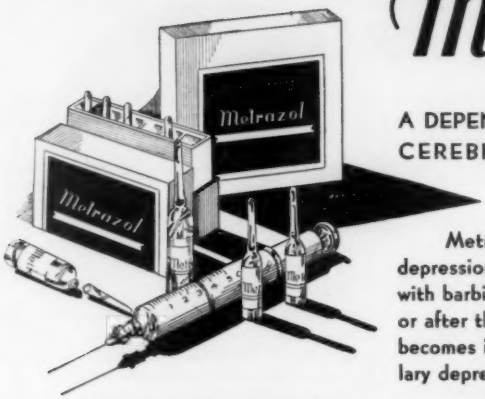

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Complete Epileptic Seizure-control; First Step in Rehabilitation

In the drug therapy of the epileptic, nothing short of *complete* suppression of seizures can rightly be called full success. Complete seizure-control is a prerequisite to the patient's return to a normally active life. Carter[1] states: "Basically all efforts should be directed toward preventing seizures and the tendency to chronic invalidism."

The management regimen should include:[1]

I. Good physical and mental hygiene.
   a) Wholesome diet; Regular bowel habits; Avoid noxious materials, e.g. alcoholics; Moderate physical activity.
   b) Help overcome feeling that epilepsy is shameful; Encourage normal work and recreation; Regular sleep without overprotection.

II. Anticonvulsant medication selected on the basis of Exact Diagnosis:

"Certain drugs are more effective in one type of seizure than they are in another, and it is necessary to use proper drugs. The dosage must be individualized for each case."[2]

Thus, the best guide in selecting medication for a patient is the type of seizures present. (Frequently several drugs in combination is most effective.)

The table shows which drugs are indicated for each type of seizure. It will be noted that the newer hydantoin, Mesantoin, is effective for *grand mal*, Jacksonian and focal seizures.

MESANTOIN DOSAGE is adjusted to the lowest level adequate to attain freedom from seizures. Start with ½ or 1 tablet daily during the first week; increase the daily intake by ½ or 1 tablet during the next week. Continue this up to optimal dosage. When another drug has not given good results, Mesantoin is added by the same procedure; then the old drug is gradually reduced.

SIDE EFFECTS — Mesantoin produces side effects in some cases: Skin and blood changes are signs of sensitivity — the drug should be discontinued. Drowsiness develops upon reaching maximum dosage.

PRECAUTIONS — Certain precautions are necessary to minimize untoward effects.

a. close check on patient — repeated visits and blood counts.
b. No Mesantoin, if white cell count below 4000.
c. caution if (1) rash or blood changes.
   (2) History of drug sensitivity.
d. discontinue drug if (1) bleeding of gums or vagina.
   (2) Sore throat

TYPE OF EPILEPSY	PRIMARY CLINICAL MANIFESTATIONS	MEDICATION	AVERAGE ADULT DAILY DOSE★	LIMITING SIDE EFFECTS	SIGNS OF SENSITIVITY
GRAND MAL	Aura followed by loss of consciousness; tonic-clonic convulsions and autonomic disturbance, e.g., in bladder function.	Phenobarbital	1¼ grs. h.s. Usual max.: 3 grs. per day	Sleepiness	
		5,5 diphenyl hydantoin	1½ grs. t.i.d., p.c. Usual max. 6 grs. per day	Diplopia, staggering (may increase petit mal)	Overgrowth of gums, body hairs; itching rash on extremities, gastric irritation
JACKSONIAN	Convulsions begin in one area and spread outwards (Jacksonian march.). No loss of consciousness.[3]	3 methyl 5,5 phenylethyl hydantoin (mesantoin)	Adults: 2 to 6 tabs. Children: 1 to 4 tabs.	Sleepiness	Full details given; see Psychomotor cross-column below
		phenylacetylurea[3]	2 Gms. per day. Max. dose 6 Gms. per day[4]	Drowsiness[3]	Central nervous system affected, nausea, vomiting and abdominal pain[5]
PSYCHO MOTOR	Period of amnesia; actions apparently purposeful but mechanical; incoordination. Mild tonic spasms. In children: "behavior problems".[3]	3 methyl 5,5 phenylethyl hydantoin[4]	Adults: 2-6 tabs. Children: 1-4 tabs.	Pharyngitis, mucous membrane bleeding, lymphadenopathy, measles-like rash with itching and fever; in severe reaction: blood dyscrasia.	
		phenylacetylurea[3]	See phenylacetylurea—above		
PETIT MAL TRIAD	Attacks: in series (rapid succession), abrupt onset, few sec. duration; no aura nor impairment of consciousness. Rhythmic twitching (e.g. eyelids).	3,5,5 trimethyl oxazolidine 2,4 dione	0.9 to 1.2 Gms.	Inability to see in a bright light. Drowsiness	Hiccough, acneform rash, leukopenia
		N methyl derivative of phenobarbital	6 grs.	Sleepiness	

★Although an average daily dose can be stated for each of these drugs, to obtain best results it is necessary that the physician determine the dose required by each individual patient for maximum control of his seizures.

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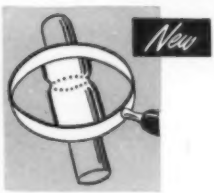

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